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FREE THROMBI AND BALL-THROMBI IN THE HEART.*

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Within the last one hundred years there have been, according to my investigation of the literature, over 30 cases of loose bodies found in the cavities of the heart on post mortem examinations. These bodies may be divided, according to their composition, into two general classes: (I.) Those consisting of material different from any of the existing elements of the blood or substances that may be directly derived from those elements, as emboli of tumor cells;[1] (II.) those made up of elements derived from the blood, as thrombi and ante mortem blood clots. I have left unconsidered all cases of the first class in this paper, but of the cases in the second class I have endeavored to find and to consult the original report in all.

It has heretofore been the custom of authors to consider these loose thrombi found in the heart in a general way and to class them all under the heading "ball-thrombi." A careful consideration of the original reports of many, in fact, the majority of these cases, shows that, so far as can be made out from the description or the accompanying illustrations, the thrombi were not "balls," but more or less irregular ante mortem blood clots. Accordingly, this second class of loose bodies in the heart may be considered under two subheadings: (a) those loose thrombi of irregular shape, size, and situation, associated with a constant pathological change in the heart, or, in other words, free thrombi, and (b) ball-thrombi.

I have herewith first reviewed the literature on free thrombi of whatever character found in the heart. I have one additional case to add, and have been able to collect fairly complete reports on three other cases that are incompletely described, or only mentioned, in the literature; and one case that has not been before published has been referred to me and I include it also.

In 1814 William Wood,[2] of Edinburgh, reported, in a letter to the editor of the *Edinburgh Medical and Surgical Journal,* the first

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*** Read by title at the meeting of The American Association of Pathologists and Bacteriologists, Chicago, April, 1911.**

genuine case of "ball-thrombus of the heart." This is practically 70 years before either those cases mentioned by v. Recklinghausen, to whom all the German authors that have written on the subject have given the credit for reporting the first case, or the spurious case of Macleod, which had a marked notoriety, were published. His description is so precise and his opinion as to how these bodies are formed, in a general way, conforms so nearly to those advanced by much later writers that I here include the greater part of his paper verbatim.

Letter inclosing history and dissection of a case, in which a foreign body was found within the heart, to Dr. Duncan, Jr., by William Wood, Fellow of the Royal College of Surgeons, Edinburgh.

Dear Sir:—I enclose an account of the principal symptoms of disease which occurred in a young girl who died, under the care of my father and myself, in consequence of an affection of the heart, together with a description of the morbid appearances discovered on dissection.

The symptoms and progress of the disease in this girl, you will perceive, differ little from those generally met with in cases where there has been found, after death, such an alteration in the structure of the heart, or of the large vessels arising from it, as must have disturbed the regularity of the circulation of the blood through that organ; the dissection, however, appears to me to be a singular and interesting one, from its affording an example, by no means of frequent occurrence, I believe, of the formation, during life, and existence for probably a great time, of loose substances, of considerable size, within one of the cavities of the heart.

All the symptoms of the disease, as well as the morbid appearances of the right cavities of the heart, may be, I think, satisfactorily explained on the principle of obstruction to the free passage of the blood through the left side of that organ; and, indeed, the principal difficulty in the case seems to be in conceiving how the circulation should have been sufficiently carried on to maintain life for any length of time, under such a degree of obstruction as must have been produced in this instance by the joint effect of the diseased mitral valves and of the foreign bodies contained in the left auricle, the former materially contracting the opening between the auricle and ventricle, and the latter retarding and diminishing the current of blood toward it; an effect which, from their situation, size, and form, these substances seem to have been well calculated to produce.

With regard to the morbid appearances on the left side of the heart the most probable supposition appears to me to be that the disease had originally existed in the mitral valves, producing diminution in the size of the ventricular openings; that, in consequence of this contraction, accumulation of blood had taken place in the left auricle, and coagula had been there formed, upon which coagulable lymph had been afterwards slowly and gradually deposited; the different substances thus formed assuming different shapes according to the relative situations in which they had been placed with regard to each other, and to the internal parts of the auricle. But whether this be or be not a true account of the formation of these solid bodies, there can be no doubt, I think, from their laminated structure, that they had existed during life.

Unfortunately in this, as in all other cases of organic affections of the heart, neither the history of the disease, nor the examination of the body after death, affords us any practical information whatever; if, however, the case appears to you worthy of being recorded as an object of curiosity, I request that it may be inserted in your Journal.

Yours sincerely, W. Wood.

A. S., a girl of 15 years of age, who had been always of rather a delicate habit, about three years ago, when walking along the street, became suddenly affected with great difficulty of breathing, and general weakness, and was so unwell that it was with difficulty she could continue her walk home. Next day she was rather better, but ever afterwards remained subject to difficulty of breathing on taking any violent exercise. In addition to this complaint she, soon after the first attack, became affected with constant strong pulsation in the region of the heart, much increased on walking up stairs or climbing an ascent. It was at this time that I was first called to see her. I found her complaining very much of uneasiness in the chest, from the constant palpitation; she could not bear her clothes at all tight, and she seemed very uncomfortable when the hand was pressed at all tightly on the thorax. The palpitation was so strong that it could be distinctly seen at a considerable distance. On applying the hand over the region of the heart strong palpitation was felt; and at a particular spot, about the size of a crown piece, a peculiar thrilling sensation was communicated to the fingers at each stroke of the heart, not easily described but somewhat resembling the effect produced on the ear by the emission of a short hissing sound at frequent regular intervals. She could lie in bed, but her sleep was disturbed by disagreeable dreams. These complaints gradually increased in severity, with the addition of fainting-fits of some duration, occurring generally three or four times in the course of every day. These were sometimes so sudden in their attack that she dropped down instantly, deprived of sense and motion; at other times, according to her friends' account, they were preceded by an involuntary contraction of the fingers and toes. These fainting-fits continued for upwards of two months, when they left her, and never again returned. Being removed to the country, I had no opportunity of seeing her for some time, but I was informed that while there, having spit up a considerable quantity of a clear watery fluid, after a severe fit of coughing, she had become considerably easier, and could take a little gentle exercise, which she had not been able to do when she left town. On her return, I found her certainly rather easier, but the strong palpitation was still constantly present. This state of comparative comfort, however, was of short duration, for very soon the symptoms became all much aggravated, with the addition of frequent spitting of blood, though in no great quantity. She was now unable to lie down, but was supported in bed by means of pillows, in nearly an upright posture. The pulse was intermittent. She had a very sallow complexion, and was extremely out of spirits. She lingered on, gradually and slowly losing strength and flesh, till the beginning of November, when she died quite exhausted, above three years from the commencement of her complaints. For many weeks previous to her death, dropsical effusion had taken place into the cellular substance of the lower extremities, and, by her friends' account, for about fifteen or sixteen days, large purple spots, of the size of half-crown pieces, had appeared on different parts of her body.

During her illness digitalis was repeatedly administered, occasionally with the effect of procuring temporary relief; the rest of the treatment consisted in regulating the diet, attending to the state of the bowels, and in occasionally exhibiting cordials.

Dissection.—Within the general cavity of the thorax there was found a very considerable quantity of bloody serum. The lungs in general were of a healthy appearance, but towards the root of one of the left lobes, there was discovered a considerable mass of a white gritty concretion.

The pericardium, which was somewhat thickened, being laid open, several ounces of clear serum were removed, and the heart brought into view, considerably larger in size than natural, the increase appearing most remarkable on the right side, the cavities of which, particularly the auricle, were much distended with blood. The heart being removed from the body, with the view of having it particularly examined, the right auricle and ventricle were laid open; in these the disease seemed to be entirely confined to enlargement of their cavities. The tricuspid and semilunar valves of the pulmonary artery were apparently in a sound state.

On splitting open the left auricle, which appeared larger than usual, the musculi pectinati were observed to be considerably increased in thickness, and there was found occupying, and nearly entirely filling up, the cavity of the left sinus venosus, a round firm body of considerable size; immediately under which, and over the situation of the opening into the ventricle, there was contained another solid substance of an oval form. A third substance, rough and irregular, had also been lodged in the auricle, but its situation could not be precisely ascertained; it lay, however, towards the ventricular opening. All these being removed, an attempt was made to pass the finger from the auricle into the ventricle, but this was found to be impossible. The left ventricle was therefore fully laid open by an incision, and, on examining the mitral valves, they were found to be much thickened, and quite opake, by their connection and situation permanently contracting the opening from the auricle into a small oval fissure, into which not even the tip of the little finger could be introduced.

The semilunar valves of the aorta were opake, and much thickened.

The substance, occupying the sinus venosus of the left auricle, when particularly examined, was found to be of a darkish red color, in form

completely spherical, measuring rather more than an inch and a half in diameter. It felt firm, but elastic; the surface was everywhere smooth and polished, but having a singularly clotted appearance. It had no connection with the surrounding parts, rolling loosely in the auricle. When cut open, after having been kept for some days in diluted alcohol, it was found to consist of a sac, one-eighth of an inch in thickness, formed of an immense number of firm smooth laminæ, which could be easily separated from each other. Within the cavity formed by this sac was contained a quantity of coagulated blood. The flat substance which lay between the round body and the opening into the ventricle was of an oval form, an inch in length and three-fourths of an inch across at the widest part. Its upper surface was of the same smooth clotted appearance with that of the former, slightly concave, so as to form a kind of superficial socket for it to roll in; the under surface, which lay over the mitral valves, was rough and irregular, containing something somewhat resembling a firm coagulum of blood in a concave depression.

In 1856 Dr. Henry Cady[8] reported three cases of "Fibrinous bodies found in the heart after death." The third and last of these cases was briefly as follows:

"A male child, about two years old, always well till about nine months before, when it suffered from a slight attack of diarrhœa. Six months later it was seized with a genuine attack of dysentery, though of only medium intensity. The child was convalescent in two weeks from the onset of the disease. After a continued state of improvement for four or five days, suddenly, in the middle of the night, having rested quietly up to that time, it was suddenly seized with a convulsion, which lasted more than four hours. Twelve hours afterwards, however, it appeared nearly as well as before the fit. The night following it had a slight paroxysm lasting about five minutes; and on the night still succeeding, one still slighter, lasting no more than half a minute. There was no more appearance of convulsive action till nearly the close of the third day from the last named period, when it was seized with a fit more severe than the first, and continued profoundly convulsed for nearly 12 hours, when death closed the scene."

Post mortem examination, made 12 hours after death, showed patches of injected mucosa and ulcerations that had not healed in the colon; considerable congestion of the blood vessels of the brain. The heart appeared normal, some "lumps of dark-colored coagula in the left side of the heart. The right ventricle was clear. The right auricle contained a small amount of dark coagulum, and in addition a small body of fleshy color, rather solid, a trifle less than an inch in length and nearly half an inch thick, in shape cylindrical. It was found lying on the tricuspid valve. . . . . This body was subsequently examined microscopically and pronounced to be fibrin." His conclusion on the subject is, "that the substances were in the heart prior to, and were the cause of death."

In 1858 Van der Byl[4] reported to the Pathological Society of London a "case of sudden death from contraction of the mitral orifice, and its obstruction, produced by a globular vegetation detached from the left auricle." The patient was a woman who had suffered for twelve months from "shortness of breath, palpitation, frequent catarrh and troublesome cough." During the three weeks preceding death she had edema of the legs, ascites, orthopnea, and frequent cough. The heart's action was rather forcible, with a mitral regurgitant bruit. She had never had rheumatism. The urine was heavy with albumin, but contained no tube casts. After breakfast one morning she suddenly fainted, became insensible, and died in a few minutes.

On section the heart was found enlarged and hypertrophied, the left auricle contained "an irregular, shaggy-looking mass . . . . . sticking in the orifice of the mitral valve. This mass "floated in water" and "assumed a sac-like appearance. . . . . . The portions required to complete the sac or capsule were found adherent to the inner surface of the auricular appendix by means of fibrinous bands and processes, which were entwined in the musculi pectinati. Three or four smaller globular bodies about the size of peas were found in the left auricular appendix, similarly fixed. On squeezing one of these, it burst, and yielded a thick greyish, purulent-looking matter, which seemed to form the contents of a capsule, similar to but smaller than the one found detached in the auricle. . . . . There was no actual organic union between any of these coagula and the walls of the auricle. The mitral orifice was contracted to four-tenths of an inch in diameter and showed warty vegetations projecting from its free margins. The aortic valve leaflets were fenestrated. The endocardium of the posterior wall of the left ventricle showed a thickened "rough patch resembling a cicatrix, about the size of a shilling." Brain, normal; no emboli in its vessels. Lungs showed infarcts the size of a hen's egg, as well as the spleen and kidneys. The latter were granular and possessed small cysts. The liver was "nodulated and granular, and on section presented radiating patches of extravasated blood." In his remarks on the case he expresses the opinion that these coagula arise from the impeded circulation caused by the contracted mitral orifice and they owe their situation in the appendix to the fact that "it is furthest from the circulating current." The chief interest is, he thinks, in "the mode in which fibrinous coagula in the heart may produce death."

In 1863 Dr. Jno. W. Ogle[5] reported briefly to the Pathological Society of London the history and post mortem findings of a case. His report is accompanied by an admirable picture of the condition, showing the case to be undoubtedly as described, and also a few remarks which demonstrate clearly that he had the correct conception of the mode of formation of these bodies. His case is as follows:

Female, age 43, admitted into St. George's Hospital, complaining of dyspnœa and anasarca, of which she had been suffering for six weeks, as well as a feeble and irregular action of the heart. Examination with the stethoscope revealed mucous râles all over the chest, egophony on the right side, a loud bruit, audible at the apex of the heart, heard distinctly with systole, doubtfully with diastole. The patient was cupped on the chest and given diuretics. No albumin was found in the urine. She improved for a time, but gradually the breathing became more hurried, with no pain however, till finally the patient died five weeks after admission.

The autopsy showed the lungs edematous, their lower parts hepatized, a quantity of fluid in the right pleural cavity. "The heart was larger than ordinary and its walls thinned. The mitral valve was reduced by thickening, and by calcareous deposits in its elements to a small buttonhole shaped aperture. The inner surface of the left auricle had several patches of fibrin attached to it; and lying loose within its cavity was a large spherical mass or concretion of fibrin weighing rather more than four drachms (Fig. I), perfectly solid throughout, and uniformly granulated in a remarkable manner on its surface, except in two places, where marks, like undulations, existed. This globular mass had also attached to it at one spot a small amount of shreddy loose fibrin. Section through this singular body showed its interior to be mainly composed of friable fibrin; but, at one part, its circumference and a certain amount also of its inner substance was formed of distinctly laminated and darker colored fibrin." (The specimen exists as a preparation in the St. George's Hospital Pathological Museum, Series VI.)

The kidneys were large, coagulated, and contained "fibrinous blocks" (probably infarcts). The suprarenals were normal in size, but as firm almost as cartilage.

In his remarks on the case he suggests that this body was no doubt produced by "the constant and free agitation of a fragment of fibrinous coagulum separated from some part of the endocardium, and uniformly increased by fresh material at its circumference, precipitated from the surrounding blood-stream. The globular form having once been assumed, its continuance during the further increase of the concretion would easily be ensured." He also is at a loss to understand how the patient continued to live as long as she did, considering the presence of this "loose body" and the narrowed condition of the mitral valve; however, as we shall mention later, it was really the narrowed condition of the valve that probably caused the formation of the thrombus.

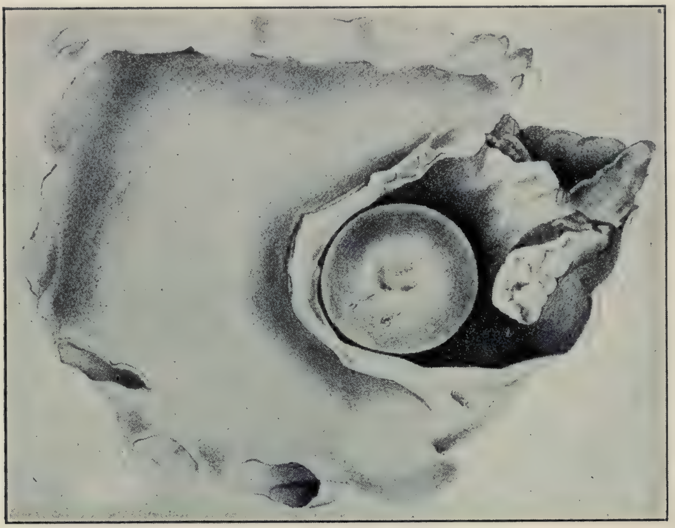

FIG. 1.—OGLE'S CASE.

A fibrinous concretion of a globular form lying loose within the left auricle of the heart.

In 1878 J. Wickham Legg[6] reported to the Pathological Society of London "Two cases of loose balls of fibrin in the left auricle with mitral stenosis." The first case was as follows:

A young man, 22 years of age, brought dead to St. Bartholomew's Hospital by the police; nothing known as to the manner of his death.

The autopsy showed a well-nourished body, no edema, face slightly cyanotic, left sided chronic adhesive pleurisy with one orange-size pleural cyst. "The heart is very large and dilated in all four cavities; the right ventricle thickened and tough. No disease of the tricuspid and pulmonary valves. On opening the left auricle, which is greatly dilated, two balls of fibrin, clearly ante mortem coagula, fall out of the auricle. They are grey and granular on the surface and marked by lines resembling the impression made by a wave on the sandy shore. Both are about the same size, that of a pullet's egg, and irregularly oval, about 15 mm. long by 30 mm. broad. The auricular appendix holds a very firm adherent, almost cartilaginous clot which shows a broken-off end projecting into the auricle. It is quite possible that one of the balls may have been joined with this clot in the auricular appendage by a pedicle, as one of them shows a surface which closely corresponds to this broken-off end. The mitral orifice is a mere chink; it scarcely admits the tip of a man's forefinger. It is beset with granulations. . . . .

"Both lungs are edematous, red and firm; spleen, large, red and firm; liver nutmeggy; kidney normal size, congested. Aorta tolerably free from atheroma but narrowed."

He then expresses the opinion that such a concretion in the heart may act as a ball valve and was very probably the cause of death in this case. He mentions Van der Byl's case as a supporting argument. The thing that most perplexed him was how the ball managed to attain such a size before death ensued. He mentions Ogle's case and then reports the following case, which he credits to Dr. Gee, as examples where the manner of death was slow.

A woman, age 43, had been in St. Bartholomew's Hospital for 15 days when she died.

On section there was no anasarca; the lungs were collapsed and the heart was enlarged, about equally on both sides; the right ventricle was dilated and hypertrophied, and the left ventricle dilated but not hypertrophied; the left auricle was greatly dilated. "The mitral orifice is markedly contracted, so as not to admit more than the tip of the finger. In the left auricle there is a round ball about an inch and a half in diameter, very elastic, very smooth, and without any trace of pedicle; that is, altogether free in the cavity." The other valves were normal. There were emboli in the kidney.

"The mode of origin of these balls of fibrin," he says, "seems very easy of explanation. In the first place there must be a considerable amount of mitral stenosis. Then a clot forms in some part of the vascular system between the radicles of the pulmonary veins and the mitral orifice; in some cases, as in the first of these, a clot is found in the auricular appendix, or, perhaps, a pulmonary infarction leading to the formation of a secondary clot in the pulmonary veins. A part of this clot, too large to pass through the mitral orifice, is broken off and therefore remains in the left auricle, instead of passing into the general system of arteries and causing infarctions of different organs, as in an unnarrowed mitral orifice might take place. Pent in the left auricle, the clot, at first of an irregular shape, is generally overlaid with fresh layers of fibrin and, from the tendency to become round which bodies possess, the clot gradually assumes a spheroidal shape."

This report of Legg's appeared five years before v. Recklinghausen published his cases, but neither he nor any of the German authors have mentioned any English case except that of Macleod.

In 1883 Macleod[7] reported a case of "A movable clot in the right auricle." His case is briefly as follows:

A man, 27 years of age, while recovering from a thigh wound, was suddenly seized with "rice water" diarrhœa and vomiting which persisted for two days and was then followed by an itching skin eruption. The patient seemed convalescent when on the fifth day he was seized with a convulsion and immediately lapsed into unconsciousness, dyspnœa, and cyanosis. A diagnosis of probable pulmonary embolism was made. Diarrhœa was persistent and involuntary, divergent squint was noted. The convulsive attack repeated itself in the evening. From it he never recovered consciousness. He had quiet delirium on the 6th day and died on the 7th day.

"On post mortem examination there were found several soft, small yellow ante mortem clots in the left side of the heart. In the right auricle was a very firm, almost cartilaginous, greyish yellow, movable clot, half as large again as a walnut, lying over the tricuspid orifice."

He thereupon expresses his belief that the first convulsive attack was brought on by a partial occlusion of the tricuspid valve by this clot; with the weakening of the heart action, the clot fell away and thus accounted for the period of improvement between the first and second attacks. He suggests that had he known the real condition he would have tilted the bed in an effort to displace the clot.

From the evidence here given we may be sure that this was not a case of ball-thrombus, and may reasonably doubt whether the clot present was the cause of death. However, the case is quoted as one of ball-thrombus by several of the German writers on this subject. I give it to make the review of the literature complete and that certain references may be more readily understood.

In 1883 v. Recklinghausen[8] in his "Handbuch der allgemeinen Pathologie des Kreislaufs und der Ernährung," in his discussion of phleboliths and venous thrombi, mentions that he had in two cases seen analogues of these bodies in the left cavity of the heart. These bodies were in both cases pale red in color, of the nature of thrombi and contained in their interior a small cavity. The mitral valve was contracted to a size smaller than the tip of the little finger. The thrombus was completely free, somewhat bulged out, but its surface was everywhere smooth. There was no pedicle, and no indication of a place where such had been attached. He believed this to be an indication that they had existed for a long time free in the blood and that they had grown by the application of new surface layers while they rolled around in the auricle. He believed they had existed first in the auricular appendix and had thereupon increased in size till they were too large to pass through the contracted mitral orifice. He gives no history with either one of the cases.

In 1885, following Hertz's[9] report of two cases of ball-thrombi and his discussion of their pathology, v. Recklinghausen[8] reviewed the subject and criticized rather severely some of Hertz's theories. He answers him sarcastically for not mentioning in two cases he had commented on in his "Handbuch der allgemeinen Pathologie des Kreislaufs und der Ernährung," which he considered the first cases mentioned in the literature. However, as shown by Welch,[10] both authors were in error on this point for having overlooked the cases of Wood, Ogle and Legg, reported in English literature. He repeats word for word his statement concerning the two cases of ball-thrombi mentioned in his book to show that Hertz's cases agreed in general with his and that he might repudiate the opinion as incorrect which Hertz's reasoning would tend to establish. He disagrees with Hertz concerning the method of formation and rounding of the ball from the loosened clot, which he accepts as the initial condition for the formation of the thrombus. This he argues is not at all one of grinding and smoothing off of rough edges and points with which the thrombus nucleus is at first covered, but rather a process of moulding, as potter's clay, rolling, and the application of new layers, and is similar to the method of formation of renal and gall stones. As to whether this thrombus can act as a ball-valve and suddenly occlude the valvular orifice, is a point on which he cannot agree with Hertz and shows the unreasonableness of his conjecture in comparison with the autopsy and clinical findings of Hertz's two cases. He notes that the funnel-shaped mitral orifices are most commonly oval in form and cannot readily be completely occluded by a round body; moreover, in the heart, in such a condition, there is no arrangement as in a ball-valve, by which the ball, should it once chance to roll into the orifice, may be held there, and so it cannot the next moment be thrown out.

He can see no reason, if the conditions during life were as found at autopsy, in the case of Macleod, why the clot should not have passed on into the pulmonary artery. He excludes it altogether from this class of thrombi, and believes that it was most probably made loose on opening the heart post mortem. He further states that the two cases mentioned by him were seen at least once each day "by most competent clinical observers," but in neither of the cases was any symptom observed that could be referred from their suddenness back to an occlusion of the narrowed orifice by the ball-thrombus.

He is firm in his conviction that no greater pathological significance can be attributed to them than to "those ball-thrombi or phleboliths arising in the lumen of vessels, varices, and cylindrical dilatations of veins."

In 1885 Hertz,* in a paper on the formation of cardiac thrombi, takes up the discussion of movable ball-thrombi and reports two additional cases. He believes them to be formed by a portion of an old thrombus in the heart cavity breaking loose and, instead of passing on out of the heart as an embolus, becoming lodged in one of the cavities by meeting with an orifice that is too small for it to pass through. Out of the literature accessible to him he was able to find only the one case of Macleod, a remark on which v. Recklinghausen subsequently criticises him in a review of his paper, because v. Recklinghausen's observations had not been mentioned. His cases are briefly as follows:

First case (Engle-Reimers), a man, 23 years of age, a journeyman tailor, who had as a child suffered from acute joint rheumatism and had suffered for a long time with palpitation of the heart and dyspnœa. After a short stay in the hospital he improved and went out of his own accord. However, he soon had a recurrence of his cardiac incompetency and had to return to the hospital.

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* *Loc. cit.*

At the time of the second admission he had a moderately good appearance, pale cyanotic face, marked edema of the lower extremities, slight ascites. The heart appeared dilated both to the right and to the left. The point of maximal impulse was in the sixth interspace and at the same point there was a distinctly palpable thrill. The heart was irregular in action and gave over the apex a loud systolic and diastolic murmur which diminished in intensity on passing upward. The second pulmonic was distinctly accentuated. The liver border was two finger breadths below the costal margin. The urine contained albumin, was diminished in quantity, specific gravity 1018. By the use of digitalis the patient's condition improved, apparently; the heart's action became more regular, its dullness diminished, and diuresis increased. Later a femoral embolus appeared and finally gangrene ot the foot developed. After having been in the hospital a little over a month there was complaint of nausea, but no vomiting. Toward evening of the same day there was an apparently rapid increase of the heart's action and of dyspnœa; cold sweats and cold extremities persisted till morning, when death followed.

Clinical Diagnosis.—Insufficiency and stenosis of the mitral valve, embolism of the right femoral artery, thrombosis of the left auricle.

At section the following conditions were noted. Dry gangrene of the right heel, embolism of the femoral and posterior tibial arteries, occlusion of the vena profunda femoris and thigh veins by old thrombi, left-sided pleurisy with effusion. The heart was markedly dilated in all its chambers, and both ventricles were markedly hypertrophied; there was atheromatous degeneration of the pulmonary artery, and the tricuspid leaflets were thickened and wrinkled. "The left auricle is dilated, the appendix thrombosed, and contains two large thrombus masses. Of these one is globular in shape with an irregular base, still fastened to the auricular appendix by a pedicle; the other is perfectly round, and is free in the auricular cavity. (Figure 2.) This last one has on its surface numerous depressions, apparently as if nibbled out; a single one of which communicates with a central softening on the inside of the thrombus mass." This thrombus measures about 2.5 centimeters in diameter. The surface, except for the defect mentioned,

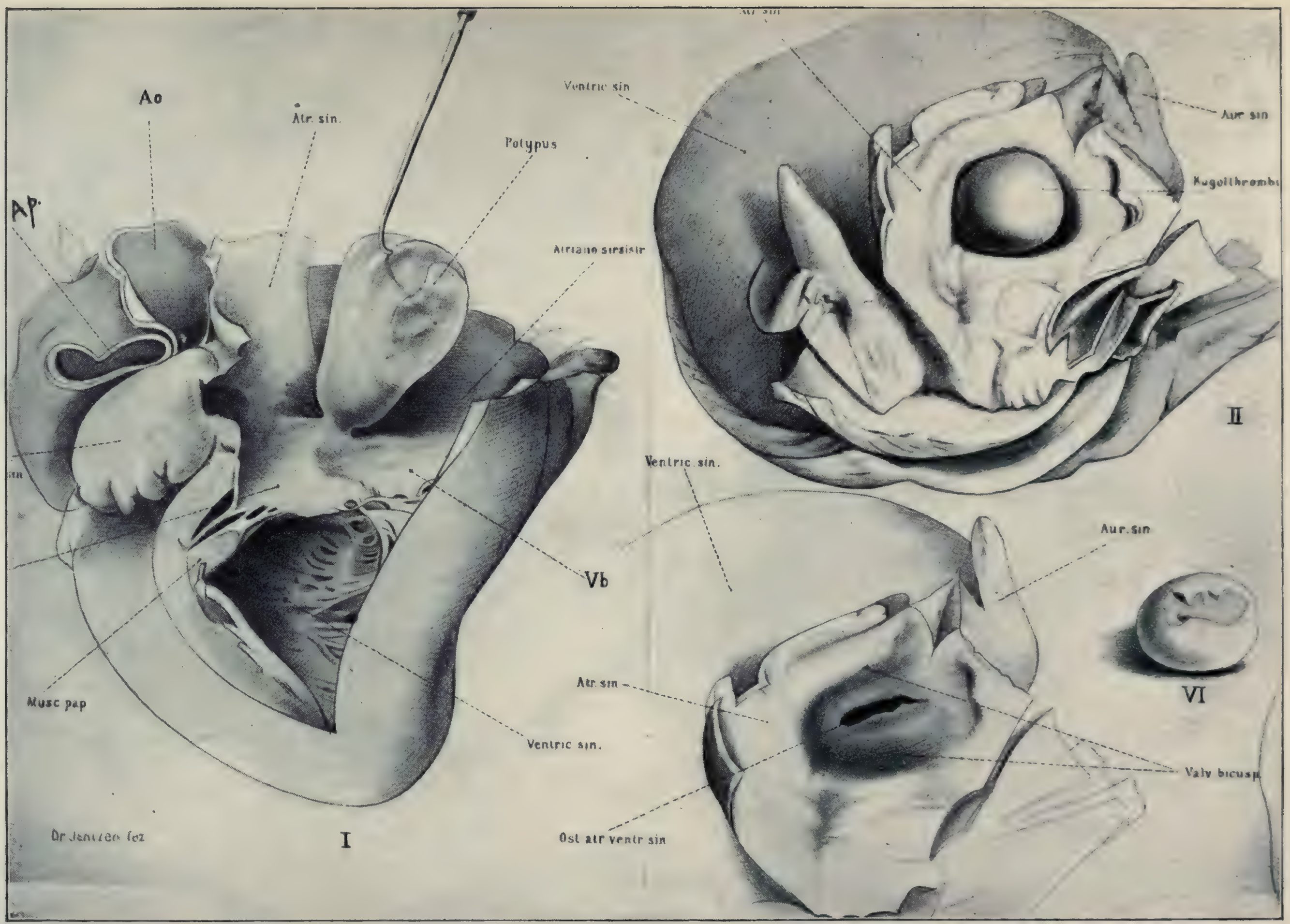

FIG. 2.—HERTZ'S FIRST CASE.

I. Pedunculated heart polyp (Case 1). The left heart is opened from the side, the polyp with a hook is drawn up. Ao = aorta, Ap = Arteria pulmonalis, Vb = Bicuspid valve.

II. Free ball-thombus (Case 1). Left atrium is opened from the side and above, the wall laid open. The ball-thrombus rested in the funnel formed by the stenosis of the valvula mitralis, and covered as a ball-valve the ostium venosum sinistrum.

III. The left auricle in the same situation drawn after the removal of the ball-thrombus.

VI. The ball-thrombus (natural size).

appears "as if fastened on a lathe and polished smooth. The inside is occupied by an irregular cavity, the walls of which are formed by a very brittle thrombus mass. . . . .

"The mitral orifice is markedly stenosed and so narrowed that one cannot get the tip of the little finger through it. Its border is beset with small coxcomb-like excrescences. Both flaps of the valve are along their free border completely fused with each other and form an apparently deep, in its lower half, rigid funnel.. . . . . The chordæ tendineæ are thickened, greatly shortened; the papillary muscles markedly developed." The aorta was narrowed and thin walled; infarcts were present in both lungs and spleen; there was a nutmeg liver, and the kidneys were scarred and fibrous. He refers to his pictures to demonstrate how the thrombus might have closed the orifice of this mitral valve "after the manner of a ball-valve."

His second case (Hansen) was a patient, sex not stated, 39 years old, affected with mania, who had suffered for years with a weak heart, diagnosed mitral stenosis and insufficiency. The patiend died suddenly after symptoms of hydrops had occurred.

On section considerable effusion was found in both pleural cavities; the heart was markedly dilated, and the right ventricle hypertrophied, containing no fibrin clots other than a ball-thrombus which was present in the left auricle and rolled out when the pulmonary veins were cut across, in removing the heart. The ball was round and measured four centimeters in diameter. It had a fibrinous compact integument, two to three millimeters thick and contained in its center a turbid, yellowish-colored fluid mixed with flakes of fibrin. At one point it showed a roughened surface, as if it had "lain on the wall of the auricle or grown upon it" at this point. The mitral orifice was contracted to an opening smaller than the tip of the little finger; both the valve flaps were drawn together and thickened.

He then gives a summary of Macleod's case. Hereupon Hertz enters into a discussion of the pathology of these ball-thrombi. His first case furnishes him with the best evidence for his theory that the rounding and smoothing of the surface of the ball had been accomplished by a process analogous to the smoothing of the pebbles on the seashore by the washing of the waves; that is, there was a grinding off of the corners and prominences of the clot by a rubbing of its surface against the wall of the auricle and the excrescences on the mitral valve. Moreover, these rubbed-off pieces were borne along in the blood stream and gave rise to the infarcts in the lungs and spleen, and the emboli in the femoral artery. The defect on the surface of the ball was most probably due to a stab by one of the valve excrescenses, he thinks. He notes the absence of any disease of the tricuspid valve in Macleod's case, but believes that the thrombus must have been formed by enormous "weakening which the heart's action during the several attacks of cholera must have suffered." He also mentions the absence of infarcts in this and his last case, but offers no explanation. His first case, he argues, furnishes a convincing proof for the origin of these thrombi from heart polypi.

In his discussion of the clinical symptoms he follows closely Macleod's case and evidently believes the thrombus produced a sudden cessation of the circulation, a point which v. Recklinghausen subsequently contested. He repeats the view promulgated by J. Wickham Legg several years before that the thrombus may act as a ball-valve. This, at first, probably by a weakening of the blood stream, enabled it to roll out of its position over the valve; afterwards, in consequence of regained strength of the heart's action, or from some unknown cause, it was again thrown into the valve orifice, with a repetition of the symptoms, convulsion, loss of consciousness, etc., which this time resulted in the death of the patient. However, the fact that death did not follow suddenly, the patient remaining alive almost two days after the first attack, shows conclusively, he believes, that the occlusion of the orifice was not complete. He notes the correspondence in the symptoms between this case and that of pulmonary embolism. He argues that the symptoms in Macleod's case were those due solely to the ball-thrombus, while in the other two cases which he reports, there was the complication of a mitral stenosis and insufficiency, and no symptoms were noted that are not commonly met with in connection with these affections.

In 1886 T. Lang[11] in Wien, writing on "The Clinical Symptoms of Free Ball-Thrombi of the Heart," on the basis of the cases of this affection reported by Hertz and v. Recklinghausen, notes the difference and coincidence of their views. He is evidently more in sympathy with the views of Hertz and takes for his principal thesis why a freely movable ball-thrombus can remain enclosed in an auricle without giving rise to severe and more characteristic symptoms than any of the cases reported had shown. In opposition to the views of v. Recklinghausen he believes the ball-thrombus can act as a ball-valve and can produce certain symptoms and that, in spite of the fact that the funnel-shaped mitral valve may be oval and the ball-thrombus round, the thrombus is elastic and more or less soft, so that if it were once caught in the orifice, sufficient pressure from above, if the valve orifice were rigid, would cause it to be moulded to the shape of the orifice and thus produce complete occlusion of the valve. Moreover, the motion of blood in the auricle and any body that may be in it during the contraction of the auricle must follow the general laws of hydraulics: accordingly, no particular arrangement for catching or holding the ball, as v. Recklinghausen intimates, is necessary. The reason the ball is not held in the orifice and that these patients can live so long in such a condition is, he believes, because the horizontal pressure necessary to hold the ball in this position is used up in overcoming the resistance presented by the stiffened mitral orifice, by its stenosis, by the great amount of friction, and, finally, by the fact that some of the muscles producing the horizontal pressure are attached to the stiffened or rigid orifice. A part of the free contents of the auricle, inclusive of the ball-thrombus, must consequently remain behind in the auricle. Still he is not willing to exclude the possibility that finally by some movement, which may not proceed from the auricular contraction, the ball may roll on the valve orifice, be pressed into it, and cause a complete interruption of the circulation.

In 1890 William Osler[12] reported from the Montreal General Hospital a case of "Large ball-thrombus, free in left auricle; mitral stenosis."

"Female, age 35, who had for twenty years been subject to attacks of shortness of breath, which had become worse within the past three years. Two years ago she had an attack of acute rheumatism, and during the past eight years she had an attack of right-sided hemiplegia, with aphasia. Speech returned in a few days, but the hemiplegia persisted for some months. Within a year she had a second attack, since which time the paralysis has persisted. When admitted there was orthopnea; face suffused; no dropsy; complete hemiplegia; the heart's action was very irregular; pulse 112, rapid and feeble; the cardiac dullness was increased; the apex beat in normal situation. There was a blowing systolic murmur in the mitral region. Temperature 101° F. Urine contained 50 per cent of albumin. The patient became rapidly worse, cyanosis increased, and death followed five days after admission.

"*Autopsy.*—Well nourished woman. . . . . Heart large, distended with blood clots. . . . . The left auricle was greatly enlarged, and contained fluid blood and clots. Among these was a ball-thrombus, ovoid in shape, the size of a small pullet egg, measuring 3.5 by 2.5 centimeters. It was quite unattached and lay free above the mitral orifice. It was firm and elastic to the touch, and on the surface greyish brown in color, and presented a little linear fibrinous elevation, but no rough spot, as if it had been adherent to the wall. It gave an indistinct sense of fluctuating as if central softening had occurred. . . . . There were no mural thrombi in the chamber. . . . . The right chambers were greatly dilated. The auricular face of the tricuspid valve presented fresh vegetations, many of them pedunculated. The walls of the ventricle were greatly thickened. The mitral orifice was very narrow, just admitting the tip of the little finger; from the auricle it looked like a little buttonhole. At the bottom there was a funnel-shaped depression. The edges of the orifice were thick, of cartilaginous consistence, and were fringed with small vegetations. The Chordæ tendineæ were short, particularly those from the anterior muscle, which was attached almost directly upon the flap. The left ventricle was small. The aortic valves were opaque and presented rows of vegetations. There was chronic congestion of lungs and spleen. No fresh infarcts. Right kidney showed several old healed scars."

He then reviews briefly Hertz's and Macleod's cases, and refers to v. Recklinghausen's statement as to his reporting the first case. He also, apparently, had overlooked Wood's, Ogle's and Legg's cases. He agrees with v. Recklinhausen that these ball-thrombi are "globular thrombi detached from the auricular appendix. . . . . It is not likely that these produce any special symptoms."

In 1890 J. Arnold[18] wrote an article concerning "The Occurrence and Consequence of Free Ball-Thrombi of the Heart." He is the first of the German authors to commit the error of giving v. Recklinghausen the credit of first describing this condition. He mentions Macleod's supposed case and the cases reported by Hertz. He notes the coincidence of the opinions of v. Recklinghausen and Hertz as to the formation of these balls "by the loosening of a former mural thrombus, and the divergence of their ideas concerning the manner of the rounding off of this detached thrombus and also the debated question as to whether it could act as a ball-valve and suddenly and completely occlude the stenosed orifice of the mitral valve, and the appearance and character of subsequent symptoms. He reviews Lang's discussion on the subject, notes the rare occurrence of these thrombi and the necessity for further observation to clear up the debated points concerning them, and thereupon reports from the clinic of Erb the following case:

A maid servant who had pneumonia five years before with no subsequent complication, no history of rheumatism or heart trouble, ten days before entering the hospital caught cold; two days later, palpitation of the heart and oppression in the chest were noted; two days later bloody colored mucus was coughed up and severe pains in the back followed.

Physical examination showed a slight cyanosis of skin of face and lips; edema of legs; normal respiration; diastolic and systolic thrill over area of maximal impulse; marked increased area of heart dullness; piping râles over the chest; a prediastolic rough murmur becoming louder and more distinct in diastole over the heart apex, indistinct diastolic murmur over the tricuspid area as well as over the aortic and pulmonary areas; second pulmonic accentuated, heart's action irregular, sometimes intermittent; splenic dullness increased; urine, acid reaction, turbid, specific gravity 1026, containing considerable albumin, a few hyaline and granular casts, many red blood cells; pulse small, soft, easily suppressed and sometimes intermittent.

Clinical Diagnosis.—Malignant endocarditis, general edema (ascites, anasarca), hypostatic pneumonia in the lower lobes of both lungs, parenchymatous nephritis, liver and spleen tumor.

Seven days after admission severe orthopnea and distress began; pulse very small, expectoration bloody and abundant, cyanosis increased, systolic murmur very distinct. Six days later there was an exacerbation of the distress and cyanosis, and the edema became so severe as to burst.

Four weeks after admission with increased distress and cyanosis the patient died.

The autopsy showed cyanosis of face, edema of extremities, face and abdomen, development and nutrition good, skeleton strong, heart free, pericardial cavity filled with clear yellow fluid, injection and ecchymosis in the pericardium.

The heart was enlarged especially as to both the auricles and the right ventricle. "In the right heart, fluid blood and fresh dark clots. In the left atrium fluid blood: on opening it one sees lying on the markedly contracted mitral orifice, a freely movable ball mass, the diameter of which is about 3.2 cm., which weighs about 9.55 grams. Its surface is in general free and symmetrical, grey-yellowish-red color; on a round place, measuring 8 mm. the superficial layer appears broken, and the ball has a knobby, somewhat spotted, surface, yet these are quite flat and completely polished; 7 mm. from the margin of this place there is a short thin filiform process (Fig. 3). By touching the ball one feels that it contains a fluid mass and the peripheral strata is very thin." The endocardium of the left auricle appeared normal. The left auricular appendix was filled with a "greyish-red clot" which was soft in the center and extended as far as the opening into the atrium and ended in "rounded off points. . . . .

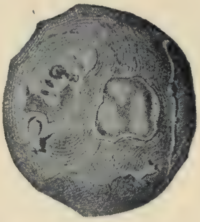

Fig. 3.—Arnold's Case.

Ball-thrombus out of the left auricle; in the middle an 8 mm. sized, round place, with which it probably lay on the orifice of the auricular appendix; on the right a narrow band-like process. Natural size.

"The mitral valve has a long oval form, measures in one direction 8 mm., in the other 6 mm. The valve flaps grown together and thickened form a firm membrane. The greatly thickened and markedly shortened chordæ tendineæ are fastened behind the line of closure." The musculature of the right ventricle was considerably thickened; that of the left ventricle, less thickened.

There were left pleural adhesions, and the thoracic cavity contained a quantity of reddish colored serum. The right pleural cavity contained gas and bloody-colored fluid and particles of fibrin; the pleura was covered partly with a thick layer of fibrin and showed a necrotic area the size of a nut. Infarcts were present in both lobes, fresh and old, one of which had undergone purulent transformation. The pulmonary artery in its large branches showed no clots.

The abdominal cavity contained a quantity of serous fluid; the spleen was enlarged and firm, of dark red color; kidneys small, enormously congested, in places contracted, capsule held firmly. The mucous membrane of the intestines and stomach was dark red and showed numerous hemorrhages; the aorta was thin walled and narrow.

"*Anatomical Diagnosis.*—Chronic endocarditis. Stenosis of the mitral valve and insufficiency. Ball-thrombus in the left atrium and adherent thrombi in the left auricular appendix. Dilation of the left auricle and right heart, relative insufficiency of the tricuspid valve. Multiple infarcts in both lungs. Necrosis and perforation of right pleura. Right pneumothorax, right sero-fibrinous pleurisy. Chronic venous hyperæmia. Chronic nephritis and insufficiency of the kidneys."

He then discusses his case, comparing its points of resemblance to and its differences from the cases reported by v. Recklinghausen and Hertz. He believes that in his case, the ball-thrombus had been formed by a loosening of a portion of the clot formed in the left auricular appendix when it had been attached either by fine threads, or over the whole area, for a period, at the round knobby place on the surface of the ball, which was about the size of the opening of the appendix into the atrium. He is not absolutely sure the thrombus had not been torn loose by manipulation of the heart at autopsy, nor is he sure whether the rounding and polishing of the surface of the ball took place while it was attached or after it became loosened and free.

As to the formation of the thrombus, as well as its subsequent loosening, he is sure the chronic endocarditis and mitral stenosis played a great part. The consequent congestion and stagnation of the blood in the left auricle, he believes, was sufficient to explain the presence of the thrombus and the stenosis of the mitral valve its retention in the cavity of the auricle.

As to whether a free ball-thrombus will or can produce, during life, any severe symptoms, he was not able to say definitely from the symptoms of his case. The marked cardiac disturbance which occurred three weeks before the death of his patient might have been produced by a transitory occlusion of the mitral valve, but the presence of the numerous infarcts in the lungs would explain the symptoms as well. That the ball was not pressed into the mitral orifice as it would have to be (as he accepts the views of v. Recklinghausen) to produce severe symptoms, is evidenced by the fact that it was not broken, and that it was so soft in the center that such pressure must necessarily have broken it.

He is not willing to confirm or deny Lang's opinion, but accepts it as a possibility that the ball, by some process, "rolls on" the orifice and temporarily obstructs the blood current; that the condition for this is most favorable during the diastole of the auricle, he believes, and that by the extreme stenosis of the mitral valve the auricle is not able to empty itself completely and consequently can exercise no horizontal pressure on such a mass as a ball-thrombus.

He concludes that, (1) With a stenosed orifice an occlusion by a ball-thrombus does not necessarily have to follow; (2) Up to that time no observations had been afforded to show that under these circumstances such an occlusion can follow; (3) When an occlusion, in general, is possible, it is brought about not by a horizontal pressure on the ball-thrombus, but by the thrombus rolling itself over or on the orifice, probably at the time of systole of the ventricle; (4) That a freely movable ball-thrombus can form and be retained in the auricle for a long time and with a normal orifice is yet to be proven.

In 1890 Fürbringer[14] demonstrated to the Medical Society of Berlin a heart obtained from a child that had died of scarlet fever, with symptoms of uremia and signs of sudden heart failure. The specimen showed about 15 pea-to-cherry sized, and even smaller, thrombi, which, partly free, partly mechanically held fast like clay-ticks to the skin, were seated on the musculi pectinati, of the right auricle. "No trace of mitral stenosis was present."

These were evidently not ball-thrombi and show, as noted by Welch,* that he had not the correct conception of the true nature of these bodies.

In 1890, also, Von Ziemssen[15] gave an account of one case of ball-thrombus along with a presentation of two cases of polypoid thrombi. He gives v. Recklinghausen the credit for reporting the first cases of ball-thrombi, mentions his cases, the so-called case of Macleod and the two cases described by Hertz. He discourses on ball-thrombi in general, following v. Recklinghausen very closely as to their origin and subsequent growth. In his case the old thrombus nucleus was easily distinguished on cross section as well as by the fine laminated covering. On the surface there were numerous small cup-like depressions and from each depression, on cross section, there was a fine cord passing to the central nucleus. These strands were distinctly older than the new laminæ, and he believed the small depressions were produced "by organization and contraction of these strands."

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* *Loc. cit.*

The clinical picture of ball-thrombi he declares the same as that of large pedunculated thrombi. He believes, from an analysis of his cases and those reported in the literature, that a probable diagnosis of autochthonous thrombosis (by which he means ball-thrombi and pedunculated thrombi) is possible under the following conditions: (1) the physical proof of a mitral stenosis; (2) the appearance of a severe obstruction to the current in the left heart (cyanosis, dyspnœa, coldness of the extremities, etc.) in a more marked degree than in mitral stenosis. He further mentions a symptom that was present in all three of his cases and in one of the cases reported by Hertz, viz., circumscribed gangrene in the feet with edema and cadaveric coldness and, especially in his cases, an obliteration of the arterial pulse of the lower extremities. He believes the gangrene might be due to an occlusion of the vessels not alone by emboli but also by arterial thrombi consequent upon the diminished peripheral blood supply.

In 1891 zum Busch[16] in his inaugural dissertation, at the Albert-Ludwigs University at Freiburg, "On the Construction of Heart Thrombi and Their Relation to the Heart Wall," argued that the disturbance in the circulation was the principal factor and that the change in the endocardium and musculature were of no consideration in the formation of heart thrombi. Following the classification of Hertz for these bodies, he briefly comments on seven cases of ball-thrombi collected "from the literature accessible to him." He gives v. Recklinghausen the honor of describing the first case and mentions besides the cases of Hertz, Macleod, v. Ziemssen and Arnold, and the controversy between the views of Hertz and v. Recklinghausen and Arnold, as to whether these thrombi may temporarily or permanently obstruct the circulation with the consequent manifestation of recognizable and distinctive symptoms.

In 1892 Schorl[17] demonstrated before the Medical Society of Leipzig a heart with marked mitral stenosis, in the left auricle of which a free ball-thrombus of the size of a hen's egg was found. Its surface was for the most part smooth, but at one point showed a rounded process. The left auricular appendix was filled with a thrombus which projected into the atrium of the auricle. He refers to the views of v. Recklinghausen and Arnold as to the mode of origin of these thrombi, and states that no clinical symptoms were demonstrated in his case.

In the discussion Curschmann stated that he had seen these ball-thrombi three times and in all three cases mitral stenosis existed and death came suddenly. There is doubt among some of the authors as to whether this is not the same case as reported by Krumholz. It is also nowhere stated, that I know of, whether this is the same case as shown in his *Stereo-scopische-photographisher Atlas* (Fig. 4) or not. However, from the above description and that accompanying his picture, I judge that it is.

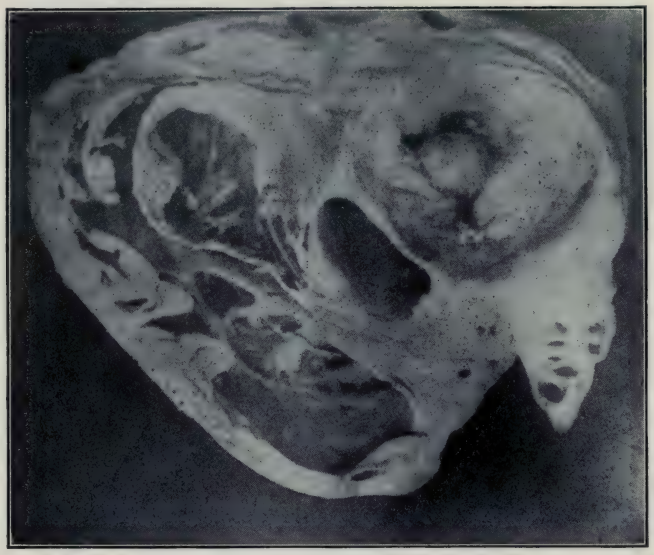

FIG. 4.—SCHMORL'S CASE.

In 1892 Redtenbacher[18] described "A Case of a Pedunculated and a Ball-Thrombus in the Left Auricle." He reviews v. Ziemssen's cases as reported at Vienna to the 9th Congress for Internal Medicine and notes that what v. Ziemssen's cases showed in separate hearts, his showed in the same heart. He then mentions v. Ziemssen's grouping of symptoms for a probable diagnosis of autochthonous thrombi and describes the following case:

A female manual laborer, 46 years of age, who was seen by him only once after admission to the hospital, in which she remained about 48 hours before death, had had scarlet fever 10 years before and rheumatism five years before admission. The rheumatism recurred after one year and was accompanied by marked palpitation of the heart and great distress. Since then she had suffered continually with palpitation of the heart and was unable to work, coming into the hospital because of increased cardiac distress.

Physical examination showed a sparely built, markedly emaciated woman, skin pale, marked edema of feet, lower extremities of a pale and livid color, smooth, shiny, and very tense; temperature markedly lowered and of death-like coldness to the touch; radial pulse scarcely palpable; heart dullness increased on both sides, a marked thrill on palpation, a distinct pre-systolic and systolic murmur over the apex on ausculation; second pulmonic strongly accentuated; liver swollen.

Diagnosis.—Extreme mitral stenosis with broken compensation, hypertrophy of the heart, possibly aortic stenosis.

Autopsy.—Marked edema and pallor of the extremities. Brain and meninges normal. The right pleural cavity contained half a liter of serum, lung free; left lung free in front, adherent behind, cavity contained quarter of a liter of bloody fluid; pleuræ covered with fibrinous hemorrhagic exudate; both lungs rusty brown in color, somewhat emphysematous and dry, pigmented; infarct in left lower lobe. Pericardium markedly dilated, contained some serum; heart enlarged three-fold, especially the right half; the right auricle taking up two-thirds of the heart's surface, hence the left ventricle appeared smaller than normal; left ventricle contained fluid blood; its wall 0.5 cm. thick, its endocardium delicate and thin; mitral valve contracted to size of tip of little finger, buttonhole shape, margins grown together, presenting a thick, shrunken, short, solid funnel; chordæ tendineæ grown together and contracted. The left auricle is enlarged to the size of one's fist and contains besides fluid blood a ball-thrombus having a diameter of 3.5 cm. This ball is round, soft, easily fluctuating. Its surface is smooth, brownish red, studded with the finest grey fibrinous threads. In the left auricular appendix, projecting into the auricular cavity, there is a thrombus fastened by a long pedicle. The endocardium is slightly thickened and dull. The bicuspid orifice was narrowed by adhesions and thickening of the valve edges to the size of one's finger; chordæ tendineæ thickened and contracted; endocardium slightly dulled and thickened; aortic cusps thin on their borders, otherwise slightly thickened; aorta somewhat narrowed and thin walled; pulmonary artery broad, cusps thin, intima here and there slightly thickened; heart muscle dark, dirty red color, very firm; marked passive congestion of liver, spleen and kidneys; cyanotic atrophy of liver; infarcts in lower pole of left kidney; chronic metritis, endometritis and colpitis; congestive catarrah of stomach and intestines.

He excuses himself for not making a diagnosis of the ball-thrombus, according to v. Ziemssen's symptom complex, by the fact that he was able to observe the case for such a short period and that the symptom of circumscribed gangrene had not developed. He believes there was a genetic relation between the pedunculated thrombus in his case and the ball-thrombus, that the ball-thrombus was at one time a "whip-shaped auricular thrombus," which developed during a period when the mitral orifice was contracted to a marked degree. It subsequently broke loose; it then lost its whip shape, could not pass the contracted orifice and by rotation and the application of fibrin, became a smooth surfaced ball-thrombus.

In 1892 T. Lang[19] reported the case of a 44 year old female who was observed while subject to attacks of severe tachicardia, coming on suddenly and without warning, and associated with fits of weakness and fainting spells. These attacks he considers due to a partial obstruction of the stenosed mitral valve and the greater part of his paper is devoted to a discussion of how and why a freely movable ball-thrombus may partially and completely for a time obstruct the circulation. He mentions v. Recklinghausen's views on this point and the cases of Hertz and v. Ziemssen. He gives no account of a post mortem examination of his case and his diagnosis must, of course, be considered very doubtful.

Rosenbach[20] in his book on "Diseases of the Heart," published in 1893, in his article on thrombosis of the heart, discusses briefly, with respect more to the clinical picture, ball-thrombi. He mentions the views of Hertz v. Recklinghausen, and v. Ziemssen and gives very briefly a case that had come under his observation. In this case there was mitral stenosis with formation of a nut-size ball-thrombus in the left auricle. Clinically there was a remarkably loud presystolic and diastolic murmur in the 2d and 3d intercostal spaces near the left sternal border, but with no whirr of mitral insufficiency at the apex.

The localization of the whirr, he believes, might be turned to account, if the possibility of an anomaly of the pulmonary orifice could be excluded.

Krumbholz,[21] writing in 1893 "Upon the Causation of Pedunculated and Ball-Thrombi," refers to the papers of v. Recklinghausen, v. Ziemssen and Hertz and gives briefly the clinical histories and autopsy findings of two additional cases.

His first case was that of a seamstress 41 years of age, who came to the hospital because of attacks, in the last week, of shortness of breath and palpitation of the heart, from which she had suffered for some time before. Twelve years before she had had for three weeks joint rheumatism, and since then the attacks had occurred repeatedly, but disappeared under medical attention.

Physical examination showed the general signs of a mitral stenosis and insufficiency, with some undetermined affection of the aortic valve. After about five weeks stay in the hospital she was well enough to be dismissed. A week later, however, she returned with the same general signs and symptoms; albumin in the urine was noted at this time. After remaining in the hospital about a month she went out, only to return again about six weeks later, when she came in for the third time. On this admission it was noted that she was very cyanotic and the dyspnœa and irregularity of the heart's action were considerable. The lower extremities were cold and edematous. A week later she died.

Post Mortem Examination.—Pericardial cavity contained about 30 cc. of serous fluid; heart enlarged. "On opening the left auricle a ball-thrombus of the form and size of a hen's egg, apparently of firm consistency and everywhere of smooth surface, is easily removed from it. On one pole is a perceptible spot on which it apparently stood, together with an attached thrombus that completely filled the auricular appendix"; mitral valve flaps thickened into a stiff narrow ring, papillary muscles hypertrophied, tendons shortened and thickened; aortic cusps, in general, thin; on the right anterior and posterior cusps there was slight thickening which prevented complete closure; right auricle dilated; the wall of right ventricle not thickened. "By subsequent examination * it appeared that the thrombus possessed an endothelial covering and had a lamellar structure." He believes there was no symptom manifest that could not have been explained by the condition found to have existed in the heart.

He then reports a case of polypoid thrombosis of the right auricle and says that also in this case there was on microscopical examination "an endothelial covering" to this thrombus.

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* Supposedly microscopical.

In 1893 Stange[22] reported from Ebstein's clinic "A Case of Ball-Thrombus in the Auricle of the Left Heart," autopsied by Orth.

He reviews the literature, and credits v. Recklinghausen with giving the name "ball-thrombus" to this class of bodies. He mentions the cases reported by Hertz, Arnold, Osler, and Krumbholz. He then presents in great detail another case which may be summarized as follows:

A male teacher, 21 years of age, was admitted to the hospital complaining that he had been suffering for five weeks with palpitation of the heart which was especially manifest after exertion and excitement. Previous history: repeated attacks of pain in stomach moving toward left shoulder; influenza one year before of eight days' duration; articular rheumatism in lower thigh with swelling, about three months before. Physical examination: medium nourished, lies on back by preference, skin of face and hands flushed and cyanotic; rapid pulse, 116; no edema; bowing of precordial region of chest; expanding pulsation between the 5th and 6th ribs inside the mammillary line; systolic thrill plainest at apex; heart more markedly dilated towards the left; pre-systolic murmur over the apex; second sound indistinct; second pulmonic accentuated; over the left auricle a systolic murmur and a loud accentuated second sound; over the pulmonary and aortic areas a systolic and diastolic murmur, also over the tricuspid valve and abdominal aorta; râles in lower posterior left lung; liver and spleen enlarged; urine contained albumin and casts; spine curved forward.

Clinical Diagnosis.—Insufficiency of myocardium . . . . ., aortic insufficiency, nephritis.

In the hospital, with rest in bed and tincture of valerian, the patient at first improved. However, about four weeks after admission, palpitation of the heart returned with pain and air hunger. This condition, in the course of a few days, was aggravated by a steadily diminishing quantity of urine and increase of albumin, by pain in stomach and vomiting, pallor, slight icterus, edema of joints, coughing and spitting up of blood. He was found dead in bed after having been known to have arisen one hour before. He was in the hospital about five weeks.

Autopsy.—The heart appeared double pointed. The long dimension seemed less increased than the width; both ventricles were dilated; right auricle markedly, the left auricle less dilated. Inside the left ventricle there was a walnut-sized thrombus that had existed free in the auricle (Fig. 5). It had a convex-ribbed surface, of dirty red color, which was marked by numerous projecting ridges, appearing as grey elevations; the other more flattened surface was slightly ribbed, and had in its center an opening out of which a papillary projection extended, giving the whole mass very much the appearance of a fungoid growth. Nowhere on the entire surface was a torn place apparent. On section it was of a grey red color through which ran numerous fine and coarse greyish red strands which took their origin from the papilla-like projection and radiated from it, fan-wise, to the surface where they projected as ridges. The thrombus was everywhere rather firm in consistency, nowhere any softening to be seen or felt. The heart muscle was thickened over the right conus, over the apex thinned to 1 mm. It was of a light brown color, flecked with yellow, especially marked in the papillary muscles. The wall of the left auricle and appendix was thickened. In between the muscle bands of the appendix there was a bean-sized, greyish thrombus, the surface of which was everywhere smooth. The tricuspid valve was practically normal in width, the flaps only along their anterior borders were a little thickened.

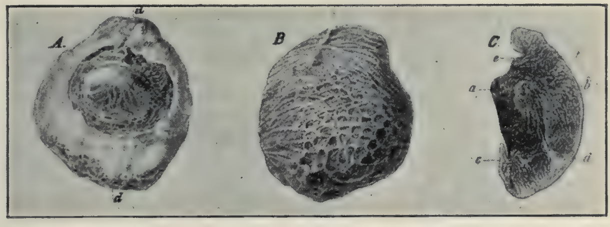

Fig. 5.—P. Stange's Case.

A and B, the two flat surfaces of the thrombus in natural size. C, cross section in natural size of A from d to d.

Anatomical Diagnosis.—Aortic endocarditis with fusion of valve cusps; retraction of the septum with marked thickening, in places calcification; destruction of the posterior valve cusps; aneurism of the sinus of the left cusp; marked dilatation with slight hypertrophy of the left ventricle; shortening of the papillary muscle trabeculæ; dilatation of the auricles, somewhat also of the right ventricle; valves fairly normal, congenital fusion of two of the pulmonary cusps; free thrombus in the left auricle, small adherent thrombus on wall of left auricular appendix; fatty degeneration of inner portion of heart muscle; hemorrhagic infarcts and emboli in both lungs; old healing infarcts in both kidneys; congestion in lungs, spleen, kidneys, liver, stomach, and intestines; slight colloid goitre; hypostatic knots in liver; slight fatty change of aortic intima; subpericardial hemorrhage; hydrops of all the serous cavities; edema of the lower extremities.

In the discussion of his case Stange admits that his is not a true ball-thrombus in the sense of v. Recklinghausen; but on the ground that, in this group, all cases of free thrombi in the heart which possess anything like a ball-shape are to be included, he thinks his case can be considered. He notes the unanimous agreement among the authors on the subject that the first essential condition for the formation of these thrombi is a stasis of blood in the heart, produced by muscular weakness or damage of the valve flaps. The thrombus thus originated in the auricular appendix grows out of it into the lumen of the auricle and, after a variable length of time and condition of growth, by some unknown process, breaks loose as a free thrombus.

Considering his own case, he believes that the tip of the papilla of the fungoid thrombus and the point of the smaller thrombus adherent in the auricle were at one time connected, and subsequently became changed by the loosening of the thrombus and the application of new masses of fibrin. He believes that the thrombus might have been free in the auricle about three days, though it had had a much longer comparatively free existence attached only by the papilla-like pedicle. This he considers corroborated by the ribbed surface and the cup-shaped depressions; if it had been free longer it would have been more spherical, reasoning according to v. Recklinghausen. He does not agree with Hertz and his "grinding off" theory for the formation of the smooth surface. The absence of softening or regressive change in the center of the thrombus he considers another point in favor of his view that the thrombus had existed only a short time free in the auricle. He compares the fine and coarse grey cords observed on section of his thrombus with those observed in v. Ziemssen's case and notes the marked difference. He believes with Zchu[23] and Aschoff[24] that these represented collections of blood platelets and the ribs were ends of blood platelet strands. He notes the difference in the condition of the mitral valve found in his case from that in most of the cases reported in the literature, but offers no explanation for it.

As to the symptomatology, he discusses at length the view held by Hertz and Lang, that such a thrombus may produce severe symptoms and even sudden death, and the opposing one of v. Recklinghausen that such a thrombus in itself may give rise to no special and characteristic symptoms. He agrees with Hertz and believes the sudden onset of marked pallor in his case, observed about three days before death, was the indication of the separation of the pedunculated thrombus and an obstruction of the circulation through the mitral orifice. He does not believe that any great diagnostic importance can be attached to v. Ziemssen's symptom of circumscribed gangrene.

In conclusion Stange states that while ball-thrombi are most commonly found in the left auricle, associated with diseased conditions of the mitral orifice, they may also be found with a comparatively normal mitral valve if their diameter is so large that they cannot pass the orifice; that they can conform themselves to the orifice, thus bringing about a temporary closure of it and severe symptoms, or complete occlusion, and sudden death. He believes that the occurrence of v. Ziemssen's syndrom is exceedingly rare.

In 1895 Bostroem,[25] writing from the Pathological Institute at Giessen "Concerning Thrombus-like Formations in the Heart," described a very old specimen he found in the museum at that place (Fig. 6). He could learn nothing of the history of the case, but judged from its size that it belonged to an adult individual; the musculature and valve leaflets were normal. In the right auricle there was fastened to the auricular septum by a very short pedicle an oval body, 5.8 x 5.3 x 5 cm. Its surface was generally smooth and showed no difference from the endocardium, with which the surface of the pedicle was continuous. On the basis of the observations of Choisy, Nuhn, Kottmeier and Prous of the occurrence of primary hemorrhage into the auricular septum, he argues that this case and many of the other cases of reported pedunculated polypi of the heart are nothing other than thrombosed varices. However, he was unable, microscopically, to demonstrate an endothelium and with a probe could find no venous connection. The description of the section of this body when compared with the thrombus in Stange's case is interesting. It was seen to be "made up of fairly uniform fibrinous masses which radiate from the pedicle towards the sides."

His article is briefly reviewed because of his hypothesis that these thrombosed varices of the heart may become detached and form the nuclei of ball-thrombi. In support of this view he refers to the cases of Macleod, Stange and v. Ziemssen.

In 1895 Eichorst,[26] in his "Pathologie und Therapie," under the heading of ball-thrombi mentions that in the preceding six years he had seen three cases at autopsy in his clinic. He gives v. Recklinghausen the credit for describing the first cases and notes that Hertz, Fürbringer, v. Ziemssen and Redtenbacher had described similar cases. He says, "These thrombi are always, perhaps, formed out of loosened parts of mural thrombi, which, aided in a rolling motion by the blood stream, while in the auricle, obtain a round form, and a lamellar structure by the application of new layers of fibrin, and gradually increase in circumference." He cites v. Ziemssen's grouping of symptoms as an aid in diagnosis.

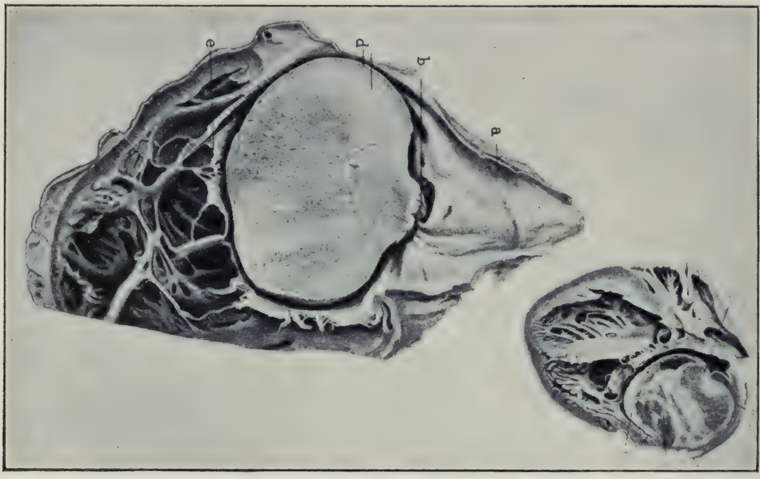

Fig. 6.—E. Bostroem's Case.

The large body fills the whole right auricle (*a*); the body has drawn out the auricular septum after the manner of a pedicle (*b*), is covered over with a thin (in the drawing all over but on the right drawn too broad) capsular membrane (*d*) which runs into the endocardium of the pedicle and consequently into the endocardium of the auricle and rests upon the lower circumference of the tricuspid valve flaps (*e*).

In 1896 Tauber[27] reported a lengthy case which may be briefly summarized as follows:

An assistant railway manager, 28 years old, had noticed swelling of his ankles for 15 years. A persistent purulent discharge from his nose had been present for eight years. Palpitation of his heart and dyspnœa on exertion had been present for four years. Three months before, the dyspnœa and palpitation became worse and accompanied by such severe edema and pain in the stomach that he sought the hospital.

On admission he was seen to be of middle size, solidly built, somewhat emaciated. The skin was pale and icteric; face and extremities cyanosed, slightly edematous; superficial veins dilated; respiration labored. The apex beat was not evident; systolic retraction in the 5th left interspace. The heart dullness was greatly increased; a systolic murmur of ringing character was heard all over the valve areas; the radial artery soft, pulse arythmic, rate 100; liver markedly swollen, its border rounded; urine turbid with urates, specific gravity 1030, contained bile pigment.

Clinical Diagnosis.—High grade mitral stenosis in the stage of advanced broken compensation.

Therapy.—Infusion of digitalis.

Four days later the temperature was normal, the edema had disappeared, the heart's action was more regular and slower, and the heart and liver were diminished in size. However, vomiting recurred and the digitalis was discontinued. Eight days after admission he vomited bile-stained material; the edema increased, and the liver became larger. This was followed by an increase in the area of the heart's dullness towards the right. Skin hemorrhages developed which increased in size and number till he died.

Autopsy.—Cardiac dilatation. "The left auricle is markedly dilated and filled with solid clots. The mitral orifice admits about the tip of the little finger; its border is ossified, with fine warty excrescences springing from it. Completely free in the auricle, lying loose in the coagula, there is a ball 3.5 cm. in diameter (Fig. 7). Its surface is smooth except at one point. It weighs 25 (?) grams and is seen on cross-section to be made up of concentric layers of grey brown red color, surrounding a boggy mass."

Anatomical Dianosis.—Chronic endocarditis with insufficiency of the bicuspid and tricuspid valves; stenosis of the mitral valve; slight stenosis of the tricuspid valve; dilatation of the right auricle and ventricle; 25 (?) gram thrombus in the left atrium with parietal affection of the endocardium; total adhesion of the pericardium; general venous stasis.

In his discussion Tauber notes a number of the cases reported in the literature and discusses his own case quite thoroughly.

Osler[28] in 1896 reported a case of this affection which was associated with sudden death. He notes the comparatively infrequent occurrence of sudden death in mitral stenosis as compared with aortic valvular disease and then describes the following case.

A young lady, age 20, came into the hospital complaining of swelling of the legs and shortness of breath. Family history not known.

Personal History.—She had diphtheria and scarlet fever 11 years before; for a year or more she had been short of breath on exertion.

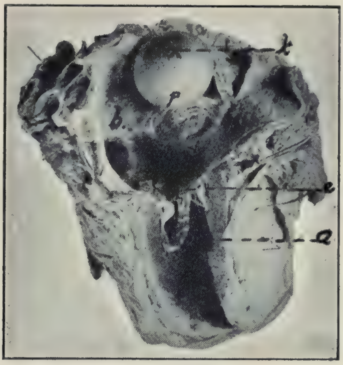

FIG. 7.—E. TAUBER'S CASE.

The left auricle open, *K*, the ball thrombus; *p*, the smooth pole; *e*, the entrance into the auricle; *a*, the stenosed orifice; *b*, the auricular endocardium.

Present Illness.—About two months before she noticed a swelling around her shoe tops which ascended to her hips. This was followed by backache and swelling in the lower portion of the spine. Lately she had had headache and puffiness of the eyes on rising in the morning; appetite poor, bowels irregular.

Physical Examination.—Appeared younger than her real age, well nourished; lips slightly cyanotic, luetic facies—saddle nose, projecting forehead, cloudiness of cornea, central incisor slightly peg-shaped. "Inspection of chest showed a heart impulse in the fourth and fifth interspaces, the maximal in the fifth, 11 cm. from the mid-sternal line. The relative dullness was at the upper border of the third rib. On palpation there was a thrill at the apex, which varied a good deal in intensity. On auscultation, the first sound was very snapping at the apex, and preceded by a rough, harsh, pre-systolic murmur, and there was a soft blowing systolic murmur passing toward the axilla. The first sound had a sharp valvular character. The pre-systolic murmur was lost in the mid-axilla. There was a good deal of echoing over a limited area in the fifth space. In the second and third left intercostal spaces the second sound was very accentuated. The second aortic sound was relatively feeble." Liver enlarged, palpable 6 cm. below the ribs; legs swollen; urine contained a small quantity of albumin and a few hyaline casts.

Under hospital care she improved, the dropsy disappeared, and the heart's action became slower, though she still had a flushed, suffused facies. She was seen the day before death and seemed quite well. She was found by a nurse very cyanotic, gave a gasp or two and died in a few minutes, after remaining in the hospital a little over three weeks.

Post Mortem Examination.—Almost the entire exposed portion of the heart was made up of the right auricle and ventricle, only a small portion of the apex of the left ventricle was apparent; the auricular appendix of the left ventricle not visible. The mitral valve segments were thickened and adherent, the chordæ tendineæ greatly shortened, the orifice just admitting the tip of the index finger; no fresh endocarditis. The left ventricle was relatively small; the right ventricle was very large and hypertrophied. The right auricle was very capacious and relatively thick walled. The left auricle was very large, the endocardium very opaque, and the wall greatly thickened. A ball-thrombus "lies loose in the left auricle, occupying the funnel-shaped space leading to the mitral orifice. It is ovoid, measuring about 3 cm. in length and at one end is roughened, indicating an area of attachment. Beyond the venous engorgement of the viscera there is no other feature of special interest. There are no lesions of congenital syphilis."

Osler believes "that the sudden death in this case was due to the dislodgment of the thrombus and a plugging by it of the narrowed mitral orifice, so that she really died of embolism of the left auriculo-ventricular orifice."

He thereupon cites a case of a three and a half year old child in which a detached sarcomatous thrombus of the left kidney had plugged the tricuspid orifice and a mass the size of a hazelnut the pulmonary orifice. He also mentions the important facts of his former case and enumerates the various forms of thrombi that are found in the heart cavities.

In 1899 Welch * in his article on "Thrombosis and Embolism" for Allbutt's System of Medicine, gave the first and most complete summary of the literature on ball-thrombi that had up to that time been presented. He was the first to give William Wood of Edinburgh the credit for describing the first case and to point out that besides Wood, Ogle and Legg had placed on record cases of this affection several years before the appearance of v. Recklinghausen's book. For a brief statement of the principal facts on ball-thrombi this is undoubtedly the best article in the literature.

In 1900 Löhlein[29] made a complete review of the literature on ball-thrombi and reported an additional case, as follows:

An extremely anemic and decrepit woman, 47 years of age, had a left-sided hemiplegia, and a stenosis and insufficiency of the mitral valve. "Broken compensation existed, which in spite of digitalis and careful attendance did not entirely disappear. There was slight atheroma present; the dependent parts were edematous. The bladder contained a large quantity of urine. The pulse was small, somewhat intermittent. This particular attack had come on suddenly, and was of quite short duration. There had been no similar attacks previously. The patient was seized as she lay quietly in bed, and just as rapidly as the symptoms had appeared, they disappeared. Besides a somewhat marked cyanosis and an enormously rapid pulse, only the anxious expression of the patient, by which the facial paralysis was evidently brought out, in any way indicated the previous injury. On the 29th of August, during a meal, an attack came on to which she succumbed. The woman, who was sitting upright, suddenly sank down, the heart made one more contraction and death ensued. During the eleven days after admission into the hospital, her cyanosis increased steadily."

On section, the heart was found of normal size; the subpericardial fat, especially on the right side, was increased; tendinous patches on the pericardium; right auricle normal; tricuspid valve normal; musculature of right ventricle thickened; pulmonary valve normal. The mitral valve was extremely narrowed, of a buttonhole shape, and quite stiff and rigid; it measured 15 x 5 cm., and was calcified along borders. The left auricle was considerably dilated and its wall thickened

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* *Loc. cit.*

to 4 mm.; the endocardium was also thickened; there was a small attached thrombus beneath the fold of the foramen ovale. The left auricular appendix was distended and filled with an old thrombus which projected into the atrium. The lower portion of this thrombus mass was torn and into it there fitted a free clot, very nearly the size and shape of a small walnut. It measured 3.5 x 2.2 x 2.2 cm., was oval, arched on one side and flat on the other. The aortic valve was normal.

He compares at length the symptoms of his case with those of the other cases reported in the literature and finally concludes that, in his case, the thrombus had been loose only a very short time.

In 1901 Wadsworth,[30] of Philadelphia, reported a case to the Philadelphia Pathological Society. He has kindly sent me his notes on this case, and as it has never been published in full, and as he tells me in a personal letter that the report that has been made of it is for the most part wrong, I take this privilege of incorporating his notes in my paper exactly as I have them from him. They are as follows:

J. H., age 40 years, white, male, single. Died April 7, 1901, Philadelphia, Pa.

A stocky medium-sized man, working in an engine factory, had been drinking freely of late, and had laid off work for about a week, probably as a result of his habits. His bed-fellow says "he died about half-past seven, without saying a word."

Making due allowance for the condition of this man the probable account of his death is briefly as follows:

While still fuddled with the liquor taken the night before, which he had been sleeping off quietly, he rolled over on waking and in changing position threw the clot into a new position in the heart and before he was altogether awake his heart stopped beating.

There were no marks of recent violence on the body and no history of anything unusual. Nor was there any history throwing light on the condition which was found.

The lungs were found in extreme congestion, the blood being dark and exuding freely from cut surface, indicating clearly that the right heart had worked strongly against obstruction in the left side.

The heart was greatly distended with dark fluid blood, especially the auricles and vessels leading to them. The muscle was in fair condition. Considerable hypertrophy of left ventricle. Valves of left side show considerable atheroma, but no vegetations. In left auricle a round clot about two inches in diameter, slightly egg-shaped but less than one-half inch difference in diameter. Surface smooth, fairly firm, slightly elastic, but before long became softer and broke, but still the fragments retained the shape of the original. Not homogeneous, one side showed yellowish granular condition.*

I can only say that the ball-clot was clearly of considerable age, not less than a month, and that the organization resembled that found in an aneurism of long standing. About and above the clot was a recent clot in the auricle.

The left auricle was greatly distended by these clots and dark fluid blood; the ball was clearly obstructing the mitral opening, causing practically complete occlusion. I am somewhat puzzled to account for the long life of this man after this had become detached and rounded into its final shape.

There was evidence in the spleen and in the kidneys of old infarcts and it is almost certain that they and the clot had resulted from an old endocarditis which had left scars on the valves of the heart, but which was not active at the time of death.

The organs showed evidence of chronic alcoholism.

The liver was hard, congested and far from normal. The pancreas was firm, mottled and had undergone considerable degeneration. The spleen showed scars, was large and firm. The stomach gave odor of alcohol and showed chronic gastritis, but was nearly empty, in a typical post-alcoholic condition. Intestines as after serious continued alcoholism. Bladder well filled, fairly normal.

Nothing further of note could be found or learned which would throw light on the condition.

(Signed) William S. Wadsworth, M. D.,
Philadelphia, Pa.

Dr. Joseph McFarland[31] has furnished me with the notes of two cases that came under his observation, which he considered cases of ball-thrombi. I also present his notes as received from him. They are as follows:

Philadelphia Hospital, 1900. No. 3126.

J. H. Men's Med. No. 13. Admitted Nov. 28, 1900. Died Dec. 3, 1900.

Primary Diagnosis.—Croupous pneumonia.

History.—J. H. White, age 56, laborer, resident of Philadelphia.

Chief Complaint.—Pain in chest, dyspnœa, weakness, anorexia, loss of weight.

Family History.—Father dead, cause unknown. Mother died of old age. One brother living and well.

Past Medical History.—Small. "Grip" several years ago. Gonorrhea many years ago. Denies syphilis. Uses alcohol and tobacco to some excess.

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* Notes as to its structure are defective because I had fully expected the person to whom the specimen was delivered to take measurements and to harden the specimen for further study.

Present Illness.—Attack of pleurisy five weeks ago. Dyspnœa, pain in chest, cough, weakness, anorexia, loss of weight.

Condition upon Admission.—Patient emaciated, rather dusky, somewhat delirious. Respiration quick and labored with retraction of the tissues of the neck. Some suppuration in the inner canthus of right eye.

Pupils equal and react to light and accommodation.

Tongue red and dry, and covered with crusts.

Pulse very small, weak and feeble; regular and of low tension. Arteries are atheromatous.

Chest and abdomen greatly emaciated. Expansion diminished particularly on right. Depressions above and below clavicles. Scales over chest.

Heart: Cardiac impulse neither visible nor palpable. Heart sounds present no abnormalities.

Lungs: Hyperresonance on left. Resonance unchanged or slightly diminished on right, anteriorly to anterior axillary line; dullness on right posteriorly, ending anteriorly at anterior axillary line. Fremitus absent over dull area and increased over rest of lungs. Egophony on left anteriorly to anterior axillary line. The line of demarkation remains fixed even when patient lies on left side. Breath sounds absent over dull area. Breathing increased over rest of lung with sounds harsh and expiration prolonged.

Abdomen: Presents nothing abnormal.

Extremities: Greatly wasted, no edema.

Ward Notes.—Nov. 28. Patient admitted in a very low state of vitality. Pulse almost imperceptible. Heart sound rapid and weak. Breathing short and rather labored.

Patient much emaciated, tongue red and dry, cheeks sunken.

Lungs: On the right side posteriorly there was dullness extending upward to about the 8th rib, and going anteriorly to about the mid-clavicular line. Over this area there was absent fremitus and breath sounds were weak and distant.

Above this area and over the other lung the breath sounds were harsh and somewhat exaggerated.

Patient has incontinence of both urine and feces.

Nov. 30. Patient steadily growing weaker. Heart sounds weak, pulse very weak. Effusion remains about the same. Needle introduced to-day and a syringeful of clear reddish fluid withdrawn.

Dec. 3. Patient gradually getting weaker, heart sounds very indistinct. Lung condition about same.

Autopsy Record.—(By Joseph McFarland, M. D., Pathologist). Dec. 4, 1900. J. H., age 56, male, white.

Clinical Diagnosis.—Croupous pneumonia.

Pathological Diagnosis.—Miliary tuberculosis both lungs. Chronic tuberculous pleuritis of right side, with adhesions and localized effusion. Miliary tuberculosis of liver, kidney and suprarenals. Ball-thrombus of heart.

Notes.—Heart. Normal in size. Right ventricle is filled with firm coagula, one of which is the size of a soup bean, dense and fibrous in structure. It is free in the cavity. The structure of the thrombus is laminated (ante mortem). Left ventricle is normal (walls, etc.) with no disease of the valves. Auricles normal. There is slight sclerosis of coronaries.

Notes on other organs had no bearing upon cardiac condition.

SECOND CASE.

Philadelphia Hospital, 1900. No. 3218.

W. F. Men's Med. No. 7. Admitted Nov. 12, 1900. Died Dec. 13, 1900.

Primary Diagnosis.—Tubercular pneumonia.

History.—W. F., white, age 66, birthplace, Philadelphia; occupation, boxmaker.

Chief Complaint.—Shortness of breath.

Family History.—Both parents died of old age.

Previous Medical History.—Measles and smallpox when a child. Had influenza three years ago. Pleurisy on right side some years ago.

History of Present Illness.—Fifteen months ago he noticed that he was not as strong as he should be and that he lost ambition for work; that he felt very weak in the morning. Five months ago he went to the Pennsylvania Hospital, and remained there for two and a half months. He was short of breath and had a cough. He says he felt much better and thought he could go out and work. He was only able to work three weeks and then had to stop on account of shortness of breath and weakness. He now has a cough. Expectoration frothy and he says it is sticky. One week ago he started coughing up blood. Has not had any night sweats but has lost considerable flesh.

Examination.—General appearance: Fairly well nourished. Sharp features.

Eyes: Pupils small and react slowly to light and distance.

Pulse: Small, rapid, regular.

Tongue: Coated irregularly; clean at the edges.

Heart: Apex one-half inch outside the nipple line. Both sounds are indistinct. Action accelerated.

Lungs: Respiration accelerated and shallow. Impaired resonance at right apex; on auscultation fine moist râles.

Abdomen: Liver dullness slightly increased.

Ward Notes.—Nov. 12, 1900. Upon admission patient complains of dyspnœa and pains in chest. Lips and finger tips slightly cyanosed.

Respiration shallow, rapid. Face is flushed. Cheek bones prominent. Emaciated. Average height. General color poor. Arteries sclerotic and beady. Pupils equal, react to light. Tongue coated.

Expansion of lungs poor, almost absent at apices. Percussion noted over right apex and over right lung posteriorly, *flat.* Over left lung fremitus increased, percussion note dull or impaired at apex. Auscultation, tubular breathing is heard posteriorly in an area about size of palm of hand at inferior border of scapula. Below and above same numerous moist râles are heard both on inspiration and expiration.

Over left apex dry râles are heard on both inspiration and expiration, do not clear up with coughing. Sputum is thick and tenacious and streaked with blood. Has no abdominal affection. Heart is slightly displaced to left; no murmurs detected. No involvement of bladder or rectum.

Nov. 15. See no change in patient's condition from note above made upon admission.

Nov. 20. Patient quite ill, appears much weaker this A. M. Expectoration still profuse, sweats at night, Repeated examination of sputum reveals no tubercle bacilli.

Dec. 1. Patient no better. Lungs present a more advanced stage of resolution than upon admission. Condition poor.

Dec. 5. Patient sinking rapidly, respiration rapid, shallow. Heart weak, feeble and in bad condition.

Dec. 13. Patient this A. M. very weak, pulse almost imperceptible. Hands and feet cold. Condition poor. Breath sounds distant. 9.15 P. M. ceased to breathe.

Urine negative for albumin, casts and sugar.

Sputum negative for *Bacillus tuberculosis*, contains streptococci and diplococci.

Autopsy Record.—(By Joseph McFarland, M. D., Pathologist). W. F., age 66, male, white. Died 9.15 P. M., Dec. 13, 1900. Autopsy 3.15 P. M., Dec. 14, 1900.

Clinical Diagnosis.—Tubercular pneumonia.

Pathological Diagnosis.—Cardiac thrombosis. Hemorrhagic infarction of lungs. Bronchiectasis. Cirrhosis of liver. Edema of lungs. Peribronchial pneumonia.

Heart: Right auricle occupied by a small thrombus. This auriculoventricular orifice admits three fingers easily (Fig. 8).

Left auricle contains large ball-thrombus (Fig. 8) and numerous recent clots.

Heart is of bovine size from dilation of both auricles and ventricles. There is hypertrophy of both ventricles and some myocardial degeneration.

Left ventricle contains a very large thrombus filling at least half of its cavity and is evidently quite old, being intimately united with the endocardium. Its center is softened and grayish in color. Rather than projecting into the ventricle this thrombus fills up its entire lower part, reducing the size of the cavity to about half. A second small thrombus projected from the wall higher up.

In the right ventricular cavity at its apex is a cherry-sized thrombus with softened center.

Lungs: Right is edematous at the apex. The upper lobe shows no interesting lesions. Middle lobe shows good-sized hemorrhagic infarction.

Lower lobe anteriorly and externally shows a consolidated area containing bronchiectatic cavities. Scattered through the lung tissues are hemorrhagic areas, infarction and pneumonia. A healed tubercle the size of a pea was found thoroughly encapsulated and partly calcified. Pulmonary artery contained a large thrombus.

Left is edematous. No hemorrhagic infarction. No pneumonic areas.

This man had an abnormally large thymus gland. The other organs contained no lesions referable to heart condition.

Dr. McFarland kindly loaned me a photograph of the thrombus in this second case (Fig. 8), and it is also pictured in his text book on Pathology (p. 32). This is, as well as his first case, evidently, on consideration, not a case of ball-thrombus; nor does the definition of ball-thrombi offered in his text book (p. 33) give a true conception of these bodies.

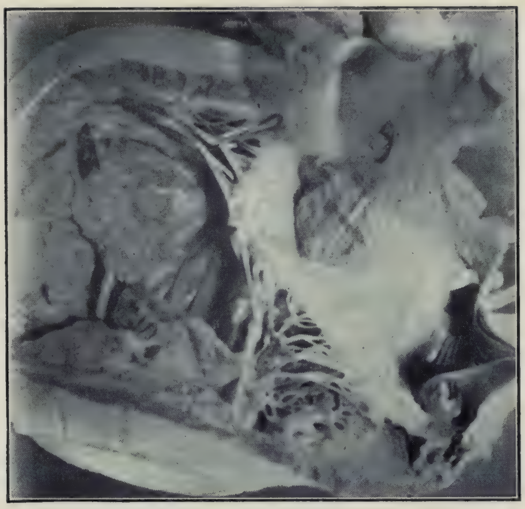

FIG. 8.—JOSEPH MCFARLAND'S CASE.

In 1904 Professor Paul Ernst[32] presented to the Zurich Medical Society a specimen of a heart of a woman 64 years of age. This showed a remarkably large and fenestrated membrane, a congenital anomaly. On this membrane in the right auricle there was a cherry-sized, round, pedunculated thrombus. He was not absolutely sure where this thrombus may have arisen, but believed the lattice-work formation of this membrane was more favorable for the formation of thrombi and that his specimen is of importance for the demonstration of ball-thrombi.

The case that was autopsied by me had been a patient of Dr. William Wier, of Cleveland, Ohio. He has kindly furnished me with the clinical history as compiled from his office record and the gynecological records of the Lakeside Hospital. I present his notes as he has sent them to me.

Mrs. J. W., age 36, was admitted to Lakeside Hospital, Cleveland, O., June 16, 1908, complaining of severe pain in the right iliac region which came on suddenly a few hours previously.

Two days previously she had consulted her physician at his office complaining of shortness of breath, palpitation, edema of the ankles, chronic cough, menorrhagia, constipation and hemorrhoids. At this time there was no abdominal pain and examination of the abdomen showed nothing abnormal. Further examination revealed the heart markedly enlarged to the left; a loud systolic murmur, loudest at the apex and transmitted into the axilla; and a marked thrill at the apex. There were a few râles over the apices and bases of both lungs. The urine showed four grams albumin per liter (Esbach) and many hyaline and granular casts, no red blood cells noted.

The family history was negative and the previous personal history showed that she had been well until seven years previously. At that time she had had a miscarriage at the fourth month: she was curetted after this but continued to flow for 14 months, when a second curetting cured the metrorrhagia. After this she improved but was never so well after the miscarriage as before. No evidence suggestive of cardiac involvement at this time could be obtained. Three years later she became pregnant and was delivered of a healthy child at term. Both cervix and perineum were torn at this time and were not repaired; as a result a descensus with a retrodisplacement developed which caused the usual symptoms, including a menorrhagia. During this pregnancy she developed "asthma," but inquiry shows that this was really failure of compensation of a damaged heart; the shortness of breath continued from this time to the present. She gave a history of an attack of "rheumatism" in November, 1907; there was no fever at that time, the pain was limited to the feet and absent when not on the feet; the attack lasted but a week and a half and at the time of this examination there was a marked giving way of the arches of the insteps; this "rheumatism" was accordingly interpreted as a symptom of flat-foot. The patient was advised as to rest, diet, etc., and was given digitalis and strychnin.

Two days before admission to the hospital she was seized with a sudden severe pain in the right iliac region together with some nausea, abdominal rigidity, slight distention and elevation of temperature to 99.5° F. Appendicitis seemed most probable and she was at once sent to the hospital. On admission examination showed 6,300,000 red cells, 16,800 white cells and hemoglobin 125 per cent. The urine was clear, yellow, sp. gr. 1030, almost solidifying on boiling from the large amount of albumin, no sugar, and microscopically many hyaline casts, leukocytes and epithelial cells; no red blood cells were, however, noted.

The patient was admitted late in the afternoon and owing to the serious heart and renal complications, operation was deferred for a few hours in the hope that improvement might occur. This did not take place and a consultation with two other surgeons was held. Appendicitis seemed the most probable diagnosis and operation was advised. This was done as rapidly as possible under nitrous oxide and oxygen anesthesia. The appendix was found markedly congested but no exudate or pus was present. Examination of the adjacent area revealed no other lesion. The appendix was removed and subsequent microscopic examination failed to show any marked inflammation.

Following the operation the failure of compensation was much increased and the patient rapidly failed. Urinalysis still failed to show red blood cells. An attempt at venesection did not prove satisfactory owing to the failing circulation and gave no relief from the damming back of the venous circulation. The temperature reached 101° F. soon after the operation, dropped to normal by midnight, then rose steadily to 104° F. just before death at 3.25 P. M. the day after the operation.

Of special interest in this case is the fact that the urine failed to show blood after the onset of the acute symptoms due to the renal involvement, the urine showing the same condition as two days before. Palpation of the right kidney during the operation showed no apparent change.

Post Mortem Examination.—Mrs. J. W., June 19, 1908. Anatomical diagnosis: Chronic valvular endocarditis with mitral stenosis and insufficiency, chronic myocarditis with general hypertrophy of the heart; arterio-sclerosis of the aorta and of the pulmonary arteries; chronic nephritis and pleuritis; ball thrombus in the left auricle; thrombosis of the inferior branch of the right pulmonary artery, and of the right renal and common iliac arteries with infarction of the right kidney; acute fibrino-purulent peritonitis and hemorrhagic pleurisy, edema and congestion of the lungs; general micrococcus lanceolatus bacteriæmia.

Body examined 12 hours after death. An adult female, well developed and well nourished, 157 centimeters in length. Rigor mortis present in the extremities and elbows, not present in shoulders and jaw. Pupils slightly dilated, but equal, scleræ moist, nose and ears normal in appearance, lips and gums cyanosed; skin generally pale, that of the face and hands somewhat tanned, pale and thin. Livor mortis is marked about the back of neck, chest, abdomen and over the buttocks. The finger nails are quite cyanotic. About the elbows are several small puncture wounds. The right thigh is larger than the left. There is no marked edema of the legs.

Thorax: The chest is well formed, long and somewhat rounded. There is a fairly marked pericardial prominence on the left side. The subcutaneous fat is moderate, the mammae pendulous, costal angle about 60°.

On opening the cavity, the right pleural cavity is found to contain about 300 centimeters of bloody fluid. The left lung is adherent to the chest wall, to the diaphragm below. [In the fat of the anterior mediastinum no remnants of thymus are made out macroscopically.] The pericardial cavity is markedly dilated to the right and especially to the left and contains an excess of fluid.

Abdominal cavity: The abdomen is rotund and prominent. On the right side, about four centimeters from the costal margin, is an operation wound, measuring about eight centimeters in length, closed above and below, packed in its central portion with two cigarette drains. The external margins of the wound are clean and adherent, by delicate fibrinous adhesions. On removing the drains their distal ends are found saturated with serum of foul odor. On opening the abdominal cavity, the subcutaneous fat is found moderate in amount, measuring one centimeter in thickness. The inner margins of the operation wound are red and injected, covered with a layer of adherent fibrino-purulent exudate. Just beneath the wound the wall of the ascending colon, adjacent peritoneum, omentum, and mesentery are covered with a layer of greenish-white fibrino-purulent material. The tissues in the region of the lower pole of the right kidney are very edematous and of a dirty reddish color. The serous membrane is in general dulled and covered with a delicate layer of sticky exudate. The stomach is markedly distended with gas, reaches 18 centimeters below the costal margin. The spleen is free, quite firm. The liver is enlarged, deeply congested, reaches 10 centimeters below the costal margin in the right mammillary line. The diaphragm extends to the fourth interspace on the right, to the fifth rib on the left.

Thoracic Organs: Left lung weighs 570 grams, measures 23 x 13 x 5 centimeters. Over the anterior portion of both lobes the pleura is thickened and of a white opaque color. Over the posterior surface of the upper lobe and the diaphragmatic surface of the lower lobe are numerous fibrous tags of adhesions. Both lobes are everywhere crepitant. No nodules are felt. On section the cut surface has a fairly uniform light red color. The lung substance is rather leathery to the feel. On pressure there is a marked exudation of bloody, frothy fluid. The bronchial mucosa is deeply injected, its surface covered with blood-tinged mucus. The pulmonary artery is thickened and shows numerous scattered patches of sclerosis. The pulmonary vein shows nothing of importance. Right lung weighs 610 grams, measures 22 x 13 x 5 centimeters. The pleura over the lower lobe is markedly thickened. The lung parenchyma shows the same general appearance as the left except that the edema and congestion are much more marked. The pulmonary artery and vein also, as well as the bronchi, show the same appearance as noted for the left side. The descending branch of the pulmonary artery, about five centimeters from its origin, shows a well-defined organizing thrombus partially occluding the vessel.

Heart weighs 400 grams. The parietal pericardium is somewhat thickened, white in color and somewhat opaque. The visceral pericardium shows scattered "milky patches" and several small ecchymoses. The right auricle and ventricle and the left auricle are markedly dilated and filled with blood. On opening the right auricle the atrium and auricular appendix are found filled with recent blood clots. The foramen ovale is closed. The tricuspid valve measures 12 centimeters in circumference. Its leaflets are thickened along their margin, firm and nodular, somewhat contracted. The left ventricle is filled with recent soft, red and "chicken fat" clots. The pulmonary valves are slightly thickened but quite competent, measuring 8.5 centimeters in diameter. From the left auricle, there extruded a large amount of soft, red, recent blood clots from the orifices of the pulmonary veins.

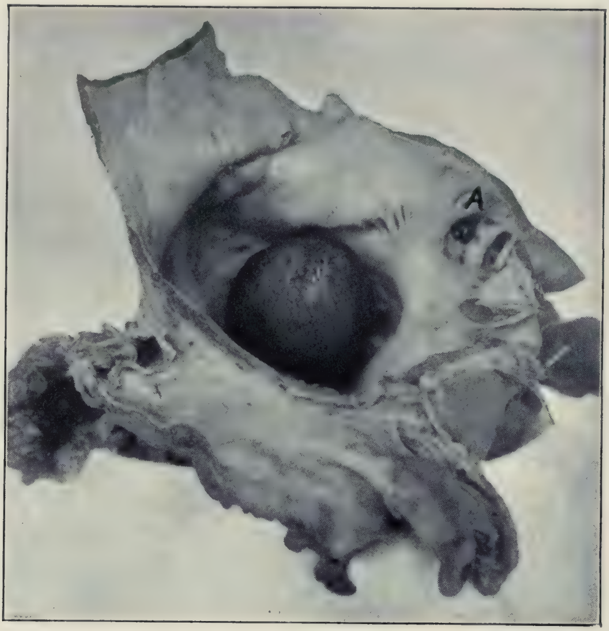

Fig. 9.—Wier's Case.

Left auricle open showing ball-thrombus in position, thickened endocardium, small adherent thrombus in appendix, *A*.

In this mass of blood clots was found a perfectly round ball-clot, (Fig. 9) which was afterwards found to measure 3.5 centimeters in diameter. Its surface is everywhere perfectly smooth and glistening, studded with *numerous pin-point size depressions of darker color surrounded by lighter material, giving it a somewhat stippled appearance. On magnifying the surface with a hand lens it is seen to be covered with a meshwork of intersecting greyish-white lines (Fig. 10). It is of a rather dark red color and of about the consistency of ordinary congealed gelatin, which it in a measure resembles. It does not fluctuate on pressure but readily yields, only to return to its former shape when the pressure is relieved. After hardening in formaldehyde (10%) this ball weighed 9 grams. On section it was then seen to be made up of (Fig. 11), an outer hull or shell about 2 to 3 millimeters in thickness, which is distinctly laminated and shows numerous whitish points and small diffuse white areas. Inside of this hull, and enclosed by it, is a fairly firm reddish white mottled mass which is somewhat polypied in outline. Its peripheral layers are partially laminated. These laminæ may be peeled off as the layers of an onion. This central mass can be separated and removed from the hull or shell (Fig. 12). Its surface then appears rather rough and uneven. The endocardium of the auricle is thickened and of a dull greyish color. In the lower margin of the opening of the auricular appendix into the atrium is a small, pea size, adherent mural thrombus (Fig. 9A). No other thrombi were present in the heart. The mitral valve is almost occluded, measuring about 0.5 centimeter in diameter. Its leaflets are fused, firm,*

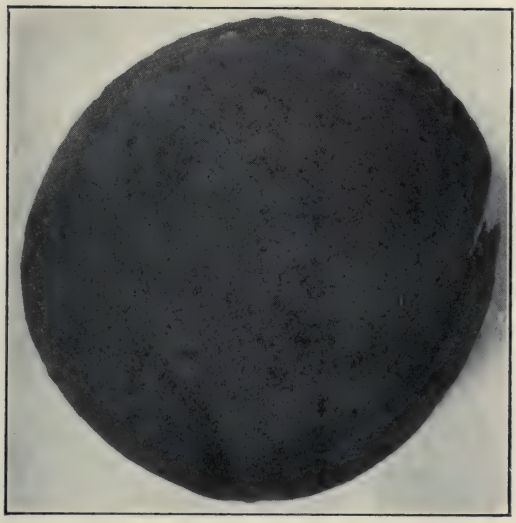

Fig. 10.—Wier's Case.

Surface of the ball-thrombus magnified about three diameters, showing the meshed outer fibrinous layer, and the numerous small depressions which produce the stippled appearance of the surface of the thrombus.

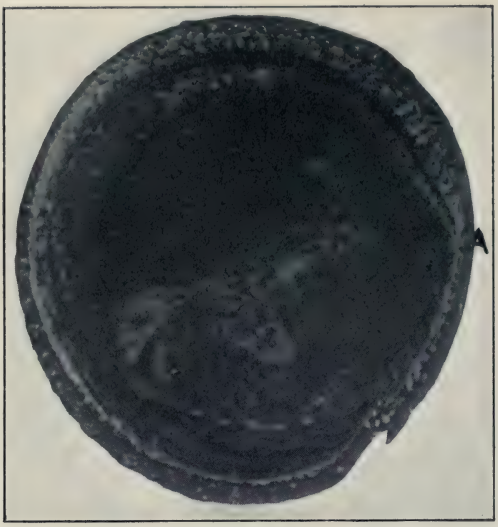

Fig. 11.—Wier's Case.

Cross section of ball-thrombus showing the outer laminated hull and the central irregular clot-mass, magnified three diameters. "*A*" appears to be the rounded original pedicle of the thrombus when it was in a polypoid state.

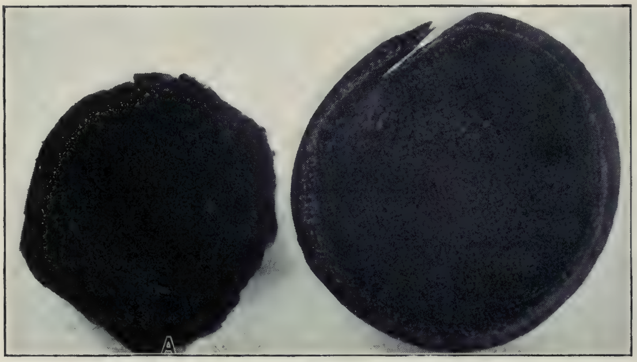

Fig. 12.—Wier's Case.

Showing the outer laminated hull with the central irregular clot-mass removed and the removed central clot-mass, magnified about one and a half diameters. At "*A*" appears to be the rounded original pedicle of the thrombus when it was in a polypoid state.

thickened and rigid, but not calcified, forming one solid membrane with a hole in it, slightly from the center (Fig. 13). The valve projects downward into the ventricle in a funnel or crater-form fashion. The wall of this funnel or crater is, however, quite irregular, containing nodular and projecting ledges.

The left ventricle was opened from below. It contains a small amount of fluid blood. Its chordæ tendineæ are thickened and contracted, the papillary muscles hypertrophied. The aortic valve measures 6 centimeters in circumference. Its cusps are thickened about their bases and around each corpus aurantius there is a firm fibrous nodule. The left ventricle wall measures 1.5 centimeters. On section the heart muscle is of greyish red color, soft, and spongy. The coronary arteries show thickening about their aortic orifices and a few delicate points of thickening of the intima about the orifices of their branches, but their walls are for the most part thin and delicate.

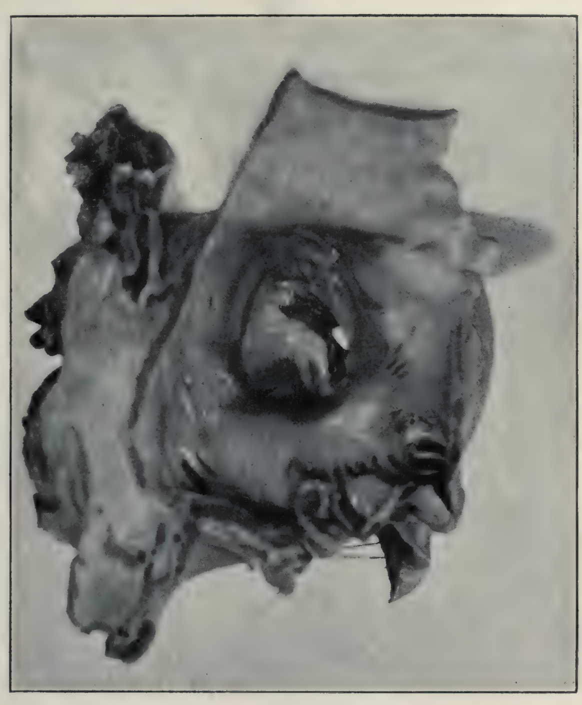

FIG. 13.—HEWITT'S CASE.

Left auricle showing the marked contraction of the mitral orifice, its decided funnel appearance with projecting points and margins.

Aorta: On the ascending and transverse portions there are scattered weals of thickening of the intima, and sclerosis. The descending portion is clear and quite elastic.

Pulmonary artery: Its intima appears in general thickened and shows numerous scattered patches of atheroma, somewhat more marked than in the aorta.

Peribronchial lymph glands: They are swollen, deeply pigmented and quite edematous.

Thyroid not examined.

Abdominal organs: Spleen weighs 190 grams. Measures 13 x 8 x 3.5 centimeters. Its surface is of a greyish purple color, capsule thickened, roughened and lustreless. On section the cut surface is of a deep red color. The parenchyma is firm. The Malpighian bodies small but distinct. The trabeculæ stand out plainly. The cut surface exudes blood abundantly on pressure.

Liver weighs 1850 grams, measures 29.5 x 24 x 7 centimeters. Its surface is of a light yellowish red color. It is firm in consistency with somewhat rounded margins. On section its cut surface has a decided nutmeg appearance.

Gall bladder distended with bile; ducts patent.

Right kidney weighs 260 grams; measures 13 x 8 x 3 centimeters. Its capsule strips readily, leaving a smooth deep red surface. It is firm in consistency. On section the cortex is seen to be markedly swollen and of a dark red color. The cut surface is more homogeneous in appearance than normal and the striations and normal markings are obscured. The pyramids are of a deeper red color than the cortex, but there is no line of demarcation between the two. The pelvic fat is increased and its surface is studded with small and large ecchymoses. It is also of a deep red color. On opening the renal artery there is found filling and occluding it a greyish red mottled organized thrombus extending from its smallest renal branches to its aortic orifice. The ureter is patent but appears quite edematous and swollen.

Left kidney weighs 175 grams; measures 11 x 6 x 4 centimeters. Its capsule strips readily, leaving a pale though injected surface, which is smooth and glistening. On section the cortex is pale. The striations are fairly well marked. The pyramids are injected and stand out boldly in contrast with the cortex. Pelvic fat is increased. Its mucosa is injected but everywhere smooth. The ureter is edematous and slightly swollen.

Adrenals: Nothing of importance noted.

Urinary bladder is slightly distended with bloody urine; its wall is slightly edematous, its mucosa injected.

Uterus: Its wall appears edematous. Its mocosa is covered with a layer of bloody mucus. There is a white mucous plug in the external os of the cervix.

Ovaries appear normal.

Stomach: Its mucosa is deeply congested and shows scattered ecchymoses. Its serous coat is slightly dulled, its wall somewhat edematous.

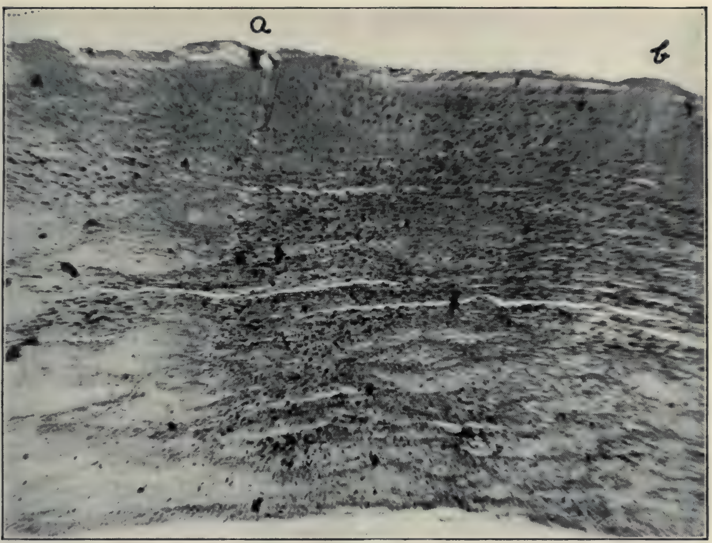

Fig. 14.—Wier's Case.

Microscopical section of the laminated hull, showing the parallel arrangement of the strands of fibrin and the leucocytes. At *a* and *b*, the surface ridges are shown, indicating the lines of the fibrin meshwork on the outer surface of the thrombus.

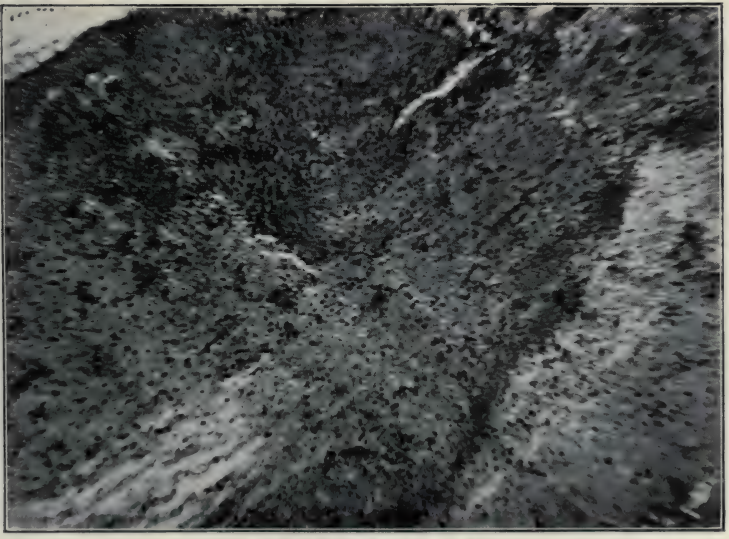

Fig. 15.—Wier's Case.

Microscopical section of the irregular central clot-mass snowing the irregular distribution of the fibrin, broken down red blood cells, and white blood cells.

Small intestines: Mucosa deeply injected and red; its serous coat is also slightly dulled and covered with small patches of fibrin.

Large intestines: Partially healed operation wound at the seat of appendix. On the ascending colon near its middle portion are fairly large patches of greenish-white fibrino-purulent exudate; otherwise it is normal.

Pancreas weighs 100 grams; measures 30 x 4.5 centimeters. The lobules are rather small.

Abdominal aorta: There are a few scattered plaques of atheromata, but it is everywhere quite elastic. The right common iliac artery from its origin in the aorta and extending into its branches is filled and occluded by an organized thrombus. Whether this thrombus arose from an embolus as well as the thrombus in the right renal artery was not made out.

Microscopical Examination.—Lungs: There is marked congestion and edema. The interalveolar wall is slightly thickened and pigmented There is a round-cell infiltration beneath the pleura. The walls of the arteries are especially thickened, some of the lumina being almost occluded. In some of the arteries are septic thrombi. There is some emphysema.

Heart muscle: There is marked hypertrophy of the cardiac cells and some fatty degeneration. The interfibrillar connective tissue is markedly increased, the walls of the smaller blood vessels thickened.

Ball-thrombus: Sections of the outer hull or shell show it to be made up of parallel strands and layers of fibrin (Fig. 14), between which are numerous leucocytes and broken red blood cells. On the surface the meshwork formation can be seen (Fig. 14, a and b) of strands and layers of pure fibrin. A section of the central mass shows it to be made up of irregularly disposed masses of fibrin (Fig. 15), between which are numerous leucocytes, red blood cells, and a quantity of detritus.

Liver: There is marked chronic passive congestion. The portal connective tissue is increased. The liver cells show parenchymatous degeneration.

Spleen: There is marked chronic congestion and increase of its connective tissue stroma. The blood vessels show thickening of their intima. The Malpighian bodies are small and ill defined.

Pancreas: The interlobular connective tissue is markedly increased, as is that in the islands of Langerhans. There are scattered areas of autolysis. In some of the islands of Langerhans there has been hemorrhage.

Right kidney: The tubular cells are everywhere swollen and necrosed except for a narrow ring around the cortex. The arteries are filled with thrombi, the veins are empty.

Left kidney: There is extensive parenchymatous degeneration of the convoluted tubules. Many of the glomeruli show fibrous thickening of their capsules, others show complete fibrosis. The inter-tubular connective tissue is increased and there is some round cell infiltration. The blood vessels have thickened walls and are everywhere markedly congested.

Uterus: Its mucosa is deeply injected. The glandular tubules are dilated, many of them cystic. The blood contains numerous leucocytes. The intertubular connective tissue is increased. The uterine wall shows marked injection of its blood vessels.

Bacteriological Report.—Smears from the abdominal cavity showed single cocci and diplococci with definite capsules (Welch's capsule stain).

Agar tubes from the heart's blood, thrombus of the renal artery, and the general peritoneal cavity gave typical growths of the *Micrococcus lanceolatus or Diplococcus pneumoniae.*

Dr. C. H. Bunting, Professor of Pathology, University of Wisconsin, recently informed me of a case of loose clot in the left auricle which he autopsied while Assistant Resident Pathologist to the Johns Hopkins Hospital, and has kindly allowed me to include it in my collection of cases.

Dr. G. H. Whipple, Resident Pathologist of the Johns Hopkins Hospital, has kindly furnished me with the notes on the case and, as it has never been published, I herewith present it as received from him.

Johns Hopkins Hospital. Autopsy No. 2449.

M. W., age 29 years. Maternity Ward. Died 3.55 P. M., Dec. 28, 1904. Autopsy, Dr. Bunting, 10.15 A. M.

Clinical History.—Admitted Dec. 27. Transferred to medical side Dec. 27, 1904. Diagnosis: Pseudocyesis—ascites from cardiac breakdown, mitral stenosis. Date of marriage, 13 years ago. Has had five children and two miscarriages. Age of oldest child 13 years; of youngest four to eight months. Date of miscarriages and period of development: abortions at two months. History of previous pregnancies and labors: patient says she was always short of breath during her pregnancies but never was troubled by any special edema. Labors were normal, the patient being attended by a midwife. Menses first appeared at 13 years. Occur every four weeks, last four days with slight pain. Date of last menstruation: says she has missed her periods for last six months. Date of first perception of foetal movements: thinks she has felt movement. History of present pregnancy: no definite history of vomiting, some headache. Patient has been short of breath for over six months and about six months ago noticed that legs had begun to swell. This swelling has gradually increased up to the present time. Patient says she has been unable to lie down for last six weeks. Has had a cough all the fall. She had typhoid fever as a girl of 12; pneumonia and pleurisy on left side three years ago; also rheumatism three years ago. Knees were affected and patient could not walk. F. H.: no tuberculosis. Condition of breasts: both breasts small, flabby and pendulous; contain no colostrum; do not look pregnant. Position and rate of foetal heart not heard. Cervix is hard. Question as to whether patient is really pregnant. Patient is too ill for even lateral measurements to be taken. She is only able to breathe when propped well up in bed.

Dec. 27. Patient rather stout woman, face slightly cyanotic, lips blue. Tongue coated, respiration labored, some cough, says she spits up mucus tinged with blood. Thorax: Right breast presents a cutaneous inflammation above nipple, in area about 3 x 6 cm. and one below nipple about same size. Lesion consists of an inflamed base with numerous red points, no pustules, very tender. Movements restricted on both sides of chest, percussion note clear; no râles on auscultation. Abdomen presents a skin lesion like that on right breast, located to right of umbilicus 10 x 15 cm. Abdominal wall edematous. Uterus ensiform and palpation of foetus impossible. Foetal heart not heard. Both legs very much swollen, in some places fluid is oozing from the skin. Diameter of ankle about 23 cm.

Dec. 27. Dr. Cole. Patient intensely cyanotic; mental condition clear, pulse extremely small, cannot be counted at wrist, heart beating 30 to ¼ of minute. Respiration labored, 28 to minute. Patient in a semi-recumbent posture, there is resonance over upper right front down to 5th rib, also resonance throughout the left front. Apex: Very well marked impulse, forcible, maximum in the 4th interspace 10 cm. from midsternal line. Dullness extends however about 12 cm. to left, above to 2d rib. To the right only reaches 4 cm. at the 4th rib. Very well marked thrill at apex and over the body of the heart apparently presystolic in times. On auscultation at the apex there is heard a well-marked sharp sound and preceding it a loud rough slightly musical murmur, most intense in parasternal line in 4th interspace. Well marked gallop rhythm at base.

Abdomen: Very markedly distended, dullness in both flanks up to the mammillary line; walls are very edematous. Transferred to medical side.

Patient was sure she was about eight months pregnant, had felt foetal movement and had even, she confessed twice endeavored to cause herself to abort. She was accompanied to the hospital by a very intelligent midwife who was sure that she had seen foetal movements on examining patient's abdomen and had heard the foetal heart.

When patient was admitted on the morning of Dec. 27, 1.10 A. M., the abdomen was so distended with fluid that positive palpation of fundus uteri was impossible, the foetal heart was not heard, however, and the breasts not having the appearance of those of pregnancy, Dr. Slemmons was in doubt as to her true condition. The patient was in such bad condition that vaginal examination was deemed unwise.

She was turned over to the medical side on Dec. 27 about 10 A. M., and at their request Dr. Slemmons made an internal examination, finding a rigid, hard cervix which also tended to confirm the suspicion that the patient was not pregnant. Bimanual examination was impossible. The patient was too ill to be removed from the maternity ward and remained here until her death at 4. P. M. on Dec. 28.

On the morning of that day her abdomen was tapped for over four litres of fluid, and then palpation showed fairly definitely that the fundus was at least not as high as the umbilicus.

At the autopsy on Dec. 29 a non-pregnant uterus was found in the normal position. The heart showed a most extreme degree of mitral stenosis, which condition was diagnosed before death.

Anatomical diagnosis.—Chronic endocarditis of the tricuspid, mitral, and aortic valves with stenosis of tricuspid and mitral orifice; hypertrophy and dilatation of the heart; thrombosis of the right auricular appendage with a free thrombus in the left auricle; general chronic passive congestion of the viscera; red atrophy of liver; general subcutaneous edema with ascites; spetic infarction of kidney.

Body: Is that of a white woman, 166 cm. in length. Rigor mortis present, well marked. Pupils equal, moderately dilated. Marked cyanosis of face, shoulders and dependent parts. Abdomen is prominent. Marked lineæ atrophical. Marked edema of the legs with slight petechial hemorrhages over the thigh.

Abdomen: The abdominal wall about the umbilicus, where all the subcutaneous fat has disappeared, is thin. The abdominal cavity contains a considerable amount of cloudy, slightly blood-stained fluid. The diaphragm reaches the fourth space on the right and the fifth space on the left.

Thorax: On removing the sternum the left lung does not appear in the incision, and just the edge of the right lung is seen. The precordial space is very wide. The tissue of the mediastinum is edematous. Both lungs are bound to the pleuræ by old fibrous adhesions which are also edematous. The pericardium seems normal.

Heart: Is large, weighing 550 grams. The pericardial surfaces are smooth and glistening. The right side of the heart is dilated, soft, post mortem clot being found in the right auricle. The auricular appendage also contains a firm, grayish-pink, ante mortem clot. The tricuspid orifice admits the tips of two fingers, and the edges of the valves are definitely thickened. The chordæ tendineæ are found shortened and the orifice appears definitely stenosed. The ventricle is dilated, its wall moderately hypertrophied, averaging about 5 mm. in thickness. The pulmonary valves seem normal. The left auricle is dilated, its wall hypertrophied, and on opening the auricle there is found free in it a laminated clot, measuring 3 x 2 x 1½ cm. The clot is somewhat lenticular in shape, being convex on one surface and showing on the under side a depression. There is about the more striated clot a small amount of post mortem dark red soft clot. The ante mortem clot has a comparatively smooth surface, and there is no rough point on it, suggesting a point of attachment to the wall of the auricle. The auricular wall also is smooth throughout. The clot fits very well the orifice of the appendage of the auricle and possibly was released from the same during the handling of the heart. However, on opening the auricle, the clot lay in the uppermost portion near the orifice of one of the pulmonary veins. The mitral orifice is extremely contracted and appears as a buttonhole slit which will not admit the tip of the little finger. It is less than 1 cm. long and about 0.5 cm. wide. The left ventricle is dilated, its wall appears somewhat atrophic and does not exceed 10 mm. in thickness. The segments of the aortic valves are thickened and curled, and apparently would present a slight interference to the outflow of blood, although the orifice admits the tip of the index finger.

Lungs: The left lung shows old edematous adhesions on the surface. Otherwise the pleura is normal. The lung itself on section is of a deep rusty red color, quite moist and showing small areas which are apparently not air-containing, and which are of a somewhat deeper color than the surrounding lung. The lung itself is tougher and firmer than normal. Its blood vessels are free from ante mortem clots, and the bronchi are congested. Right lung resembles the left.

Spleen measures 13 x 9 x 4 cm. and weighs 220 grams. The capsule is slightly thickened and adherent to the diaphragm. On section the fibrous framework is slightly increased, pulp excessive in amount, and of a dark purplish-brown color, Malpighian corpuscles small, but distinctly visible. The organ is extremely firm.

Liver measures 24 x 18 x 9 cm., the surface is irregular, roughened. Capsule is thickened, especially over the lower part of the right lobe. The edge is somewhat rounded. The cut section is very deeply congested. In the right lobe there are large areas in which the lobules appear almost entirely atrophied, the tissue appearing like sinuses filled with blood. In other parts of the liver there are large, irregular, yellowish nodules which bear no definite relation to the architecture of the organ. The gall bladder is normal. The bile ducts are patent.

Kidneys: Left kidney measures 12 x 6 x 4½ cm. Over its anterior surface it is firmly adherent to the surrounding fatty capsule, which contains definite signs of an acute inflammation. On stripping back this fatty capsule there are found on section of the kidney several irregular, yellowish areas surrounded by areas of congestion and hemorrhage. These yellow areas are much softened and are adherent to the tissue above. On section of the kidney one finds these yellow areas to extend into the substance of the kidney as opaque, yellowish areas, surrounded by a dark purplish red halo. The largest of these infarcts is about 4 cm. long by about 2 cm. wide. Except over the areas of infarction, the capsule strips fairly easily, being, however, somewhat adherent over a few, small depressed areas. The cortex is slightly wider than normal, and of a somewhat rusty color. The vessels are much injected in the cortex and medulla. Right kidney measures 12½ x 5½ x 4 cm.; resembles the left in general particulars except that it does not contain any areas of infarction.

Stomach shows marked congestion, also submucous hemorrhages, and the surface is thickly coated with mucus. There do not appear to be any areas of erosion or of ulceration.

Pancreas is deeply congested, but otherwise appears normal. Aorta shows a few patches of sclerosis.

Uterus, appendages: Appear normal except for congestion and slight uterine hemorrhage.

Intestine is injected throughout its length and shows numerous small hemorrhages at the tips of the transverse folds. Otherwise the intestine is normal.

Microscopical Notes.—Heart: Fibres are large, enormous nuclei, fragmented. Interstitial tissue is somewhat increased in patches.

Lungs show chronic passive congestion.

Liver shows marked chronic passive congestion, also focal necroses of liver cells infiltrated with polymorphonuclear white blood cells. Section No. 2 shows also coarse bands of connective tissue crossing liver and including compressed cells in its meshes.

Spleen shows congestion of vessels and pulp.

Kidneys: Tubules show swollen, granular, epithelial cells. There is congestion of vessels and glomeruli, dilatation of glomerular capsular spaces with albuminous precipitate, slight increase in interstitial tissue. Section No. 2 shows anæmic infarction.

Pancreas shows slight chronic interstitial pancreatitis.

Perirenal tissues show an acute inflammatory exudate.

Breast shows inactive state of gland, leucocytic thrombus in neighboring tissue.

Dr. G. Y. Rusk [33] has recently reported a "ball-thrombus in an aneurysmal dilitation of the ventricle." I have endeavored to secure further details of this case, but so far have not been successful.

Summary of the Cases.

Enumeration.—It may be seen from the attached table that, including the additional cases which I have here presented, I have been able to collect 35 cases of loose thrombi found in the heart. In 20 of the cases (Wood, Cady, Van der Byl, Ogle, Macleod, Hertz's two, Osler's two, Arnold, v. Ziemssen, Redtenbacher, Krumbholz, Stange, Tauber, Löhlein, McFarland, Wier, and Bunting), there is a satisfactory clinical history. In seven of the cases (Legg's second, v. Recklinghausen's two, Fürbringer, Rosenbach, Schmorl, and Rusk), the clinical history is very short and incomplete. In six of the cases (Curshmann's three and Eichorst's three), it is only stated that the cases had been seen. It is possible that some of these cases had already been reported. In two of the cases (Legg's first and Wadsworth), the patient was not seen until after death.

Sources of the Cases.—Scotland, 2; England, 4; Canada, 1; United States of America, 7; Germany, 21.

Sex.—In 21 of the cases the sex is specified. Of that number 12 were females, 9 were males.

No.	Date.	Author and Source.	Sex.	Age.	Occupation.	Status.	Duration of Heart Affection.	Character of Exitus.	Condition of Mit Valve.
1	1814	Wood: Edinb. M. & S. J., 1814, X, 50.	F.	15 yrs.		Thin, pale.	About 3 yrs.	Gradual.	"Much thickened quite opaque; manently contr ing the open from the au into a small oval sure not admit the tip of the li finger."
2	1856	Cady: Boston M. & S. J., 1856, LIII, 477.	M.	2 yrs.		Slightly emaciated.		Comparatively slow, 12 hours.	
3	1858	Van der Byl: Trans. Path. Soc., London, 1858, IX, 89.	F.	25 yrs.			About 12 mos.	Very sudden.	Measured 4 inches diameter.
4	1853	Ogle: *Ibid.*, 1863, XIV, 127.	F.	43 yrs.			About 11 wks., apparently.		Reduced by thick ing and calcar deposits in its ments to a but hole shaped a ture.
5	1877	Legg: *Ibid.*, 1878, XXIX, 49.	M.	22 yrs.		Well nourished; face slightly cyanotic.	Brought dead into St. Bartholomew's Hospital and examined 25 hours after death.	Sudden.	Mere chink, scar admitting tip man's forefinger; set with gran tions.
6	1877	Legg: *Ibid.*, 1878, XXIX, 49.	F.	43 yrs.			Under observation 15 days.	Slow.	Greatly contracted as not to ad more than the of the finger.
7	1882	Macleod: Edinb. M. J., 1883, 696.	M.	27 yrs.		Recovering from wound. Low grade of health.	Under observation 7 days.	Slow.	

	Character of Free-Thrombus.						Signs of Former Attachment.	Remarks.
	Size.	Weight.	Surface.	Consistency.	Situation.	Section.		
al.	More than 1½ inches in diameter.		Everywhere smooth and polished.	Firm but elastic.	Left auricle.	An outer sac of 2 to 3 mm. in thickness; formed of a number of firm laminæ; easily separated from each other and surrounding an irregular clotted mass.	Not present.	There was a second, irregular-shaped loose clot also present and lying over the mitral orifice and a third of rough and irregular shape.
-	1 x ½ inches.			Rather solid.	Right auricle.			This case in some respects resembles the case of Macleod.
r.	Pigeon's egg.		Shaggy.	Apparently soft.	Left auricle.	Apparently soft center.	Present.	From the description it is quite evident that this thrombus was detached only a short time before death. Death was considered due to mitral embolism.
l.	Large.	4 drachms.	Uniformly granulated with two indentation marks.	Solid throughout.	Left auricle.	Composed of friable fibrinous inner substance with a distinctly laminated and darker colored circumference.	Present.	The picture of this thrombus and its situation is the first and one of the best found in the literature.
	About size of pullet's egg, 15 x 30 mm.		Gray and granular ribbed.		Left auricle.		Present.	This case showed two balls of about the same character and size except that one showed a surface markedly resembling a broken-off end of the auricular thrombus. Legg discusses a possible ball-valve action.
	1½ inches in diameter.		Very smooth.	Elastic.	Left auricle.		None.	As noted by Welch, Legg had a clear conception of the formation of these thrombi and was the first to argue that they might act as "ball-valves."
	Half as large again as a walnut.			Very firm, almost cartilaginous.	Right auricle.			This case, apparently, has had the widest circulation and has been known by a larger number of physicians than any other case of these loose thrombi in the heart that has been reported.

No.	Date.	Author and Source.	Sex.	Age.	Occupation.	Status.	Duration of Heart Affection.	Character of Exitus.	Condition of Mitral Valve.
8 9	1888	v. **Recklinghausen:** Handb. d. allg. Path. d. Kreislaufs, etc., 1893; Deutsches Arch. f. klin. Med., 1885, XXXVII, 495.	Two cases with no history. (In a second article it is stated that these cases were examined at least twice a day but at no time showed any symptoms that pointed to an occlusion of the mitral valve by the thrombus.)						Extreme stenosis; co tracted to the si of the tip of th little finger.
10	1885	Hertz: Deutsches Arch. f. klin. Med., 1885, XXXVII, 74.	M.	23 yrs.	Journeyman tailor.	Moderately nourished, face pale and cyanotic.	Rheumatism in childhood. Under observation about one year.	Apparently, gradual.	Markedly stenosed, as not to adm the tip of the litt finger; borders b set with coxcom like excrescences.
11	1885	Hertz: *Ibid.*		39 yrs.			Suffered for years with weak heart. Under observation 4 mos.	Sudden.	
12	1890	Osler: Montreal M. J., 1897, XXV, 729.	F.	35 yrs.			Subject to attacks of shortness of breath for 20 yrs.	Rapid.	Very narrow, just a mitting the tip the little finge buttonhole appea ance; edges of ca tilaginous consis ency; fringed wi small vegetations.
13	1890	Arnold: Ziegler's Beitr. f. path. Anat. u. f. allg. Path., 1880, VII, 29.	F.	23 yrs.	Maid servant.	Well developed and nourished.	4 wks.	Gradual, with increasing cyanosis and edema.	" Long oval form 16 x 8 mm. Val flaps thickened a grown together.
14	1890	v. Ziemssen: Congress f. inn. Med., 1890, 281.					Apparently a long time.		Stenosed.
15	1890	Fürbringer: Deutsche med. Wchnschr., 1890, XVI, 505.	Child died of scarlet fever with uremia and signs of heart failure.					Sudden.	No trace of stenosi

Character of Free-Thrombus.							Signs of Former Attachment.	Remarks.
Form.	Size.	Weight.	Surface.	Consistency.	Situation.	Section.		
Ball.”	“Small walnut.”		Somewhat bulged out but everywhere smooth.		Left auricle.	Contain small cavities.	None.	He characterizes them as always pale red and containing small cavities. His description is considered by all the German authors that I have consulted as the first to record the condition of ball thrombus.
m- letely ound.	2.5 cm. in diameter.		Numerous “nibbled out” depressions, but smooth and polished.	Apparently soft.	Left auricle.	Soft center connected by one depression with the surface.	Present.	Associated in the same cavity with this spherical thrombus was a pendunculated thrombus “still fastened to the auricular appendix.” This was of a blunt shape. He notes particularly the “funnel shape” of the mitral valve.
ll ound.	4 cm. in diameter.		Elastic integument at one point showing a rough surface.	Distinctly fluctuating.	Left auricle.	2 to 3 mm. thick membrane and a fluid content of turbid yellowish color mixed with coagulated flakes.	Present.	It is noted in this case that the valve flaps were drawn together suggesting that there was a funnel shape to it also.
oid.	Small pullet egg, 2¼ x 3½ cm.		Greyish-brown color; small linear elevation.	Firm and elastic; indistinct fluctuation.	Left auricle.	Probably central softening.	None.	The funnel appearance of the mitral orifice when viewed from above is here also mentioned.
Ball nass.”	3.2 cm. in diameter.	9.55 drachms.	Grey-yellowish red color.	Soft and fluctuating.	Left auricle.	Apparently thin walled with fluid contents.	Present.	A very good picture of the thrombus accompanies this article.
lmost vheel ound.	Small walnut.		Perfectly smooth with numerous small cup-shaped excavations.	Firm.	Left auricle.	Central nucleus covered by fine laminated layers, with fine cords extending to each cup-shaped depression on surface.		He expresses the opinion that with (1) the physical proof of mitral stenosis; (2) the appearance of cyanosis, dyspnœa and coldness of extremities; (3) and circumscribed gangrene of the feet, a probable diagnosis of pedunculated or ball thrombi can be made.
	Pea to a cherry.			Fluctuating.	Right auricle.	Soft center.		Evidently, as in McFarland’s and Cady’s cases, these were not ball thrombi.

No.	Date.	Author and Source.	Sex.	Age.	Occupation.	Status.	Duration of Heart Affection.	Character of Exitus.	Condition of Mitral Valve.
16	1892	Redtenbacher: Wien. klin. Wchnschr., 1892, V, 688.	F.	46 yrs.	Laborer.	Emaciated; medium development.	4 yrs.	Rapid.	Contracted to size little finger; bu tonhole shape; ma gins grown together; presenting thick, shrunke short, solid, funn appearance.
17	1892	Schmorl: Schmidt's Jahrbuch, 1892, CCXXXV, 110.	No clinical history given other than: No symptoms which pointed to an interference with the circulation by the ball thrombus were demonstrable.						Stenosed.
18 19 20	1892	Curshman:	In the discussion of Schmorl's case he stated that he had seen three cases. Mitral stenosis was present and death was sudden.					Sudden.	Stenosed.
21	1893	Rosenbach: Die Krankheiten d. Herzens, 1893, I, 180.			No history.				Stenosed.
22	1893	Krumbholz: Arb. a. d. med. Klin. zu Leipzig, 1893, 328.	F.	41 yrs.	Seamstress.		Sometime.	Slow with increasing cyanosis.	Thickened along th line of closure, an changed into a sti narrow ring, admitting a pencil.
23	1893	Stange: Arb. a. d. path. Inst. zu Göttingen, 1893, 232.	M.	29 yrs.	Teacher.	Medium nourished.	6 wks.	Apparently, sudden.	Congestion of liver stomach and intestinal tract; sligh colloid goiter, hyperplastic knots i liver. Slight fatt change of aorti intima; sub-pericardial hemorrhage hydrops of all serous cavities; edem of lower extremitie
24 25 26	1895	Eichhorst: Pathologie u. Therapie, Zurich, 1895, 121.	Mentions that he had seen three cases.						

Character of Free-Thrombus.							Signs of Former Attachment.	Remarks.
orm.	Size.	Weight.	Surface.	Consistency.	Situation.	Section.		
nd.	3½ cm. in diameter.		Smooth, brown-red, studded with fine fibrinous threads.	Soft, easily fluctuating.	Left auricle.	Apparently softened center.		The statement concerning the funnel shape of the mitral orifice is also noticeable in this case.
l.	Hen's egg.		Smooth.		Left auricle.		Present.	There is a question whether or not this is the same case as was reported by Krumbholz.
					Left auricle.			
l.	Nut.				Left auricle.			He notes that in this case the characteristic whirr at the apex for mitral insufficiency was absent, and thinks that it might be turned to account if a possible abnormality of the pulmonary valve could be excluded.
l.	Hen's egg.		Everywhere smooth.	Apparently firm.	Left auricle.	Apparently showed an endothelial covering and was laminated.		The endothelial covering for the thrombus in this case is remarkable. This is most probably an error that rose from a misinterpretation of the appearances seen under the microscope as explained in this article, see Fig. 16.
ah- om or ngi- rm.	Walnut 3.4 x 8.1 x 1.7 x .8 cm.				Left ventricle.		Present.	
l.								

No.	Date.	Author and Source.	Sex.	Age.	Occupation.	Status.	Duration of Heart Affection.	Character of Exitus.	Condition of Mitral Valve.
27	1896	Tauber: Jahrbuch d. Wiener k. k. Kranken Anstalten, Wien u. Leipzig, 1898, 1896, V, 348.	M.	28 yrs.	Asst. railway manager.	Somewhat emaciated.	About 4 yrs.	Apparently sudden.	Stenosed; about admits tip of littl finger.
28	1891	Osler: Johns Hopkins Hosp. Rep., 1891, II, 56.	F.	20 yrs.	Bookbinder.	Looks younger than her age; well nourished.	A long time; under observation 25 days.	Died in a few minutes after a gasp or two.	Stenosed, just admitting tip of inde finger.
29	1900	Löhlein: Inaug. Dissertation, Univ. of Giessen, 1900.	F.	47 yrs.		Extremely decrepit and anemic.	Under observation 11 days.	Sudden.	Stenosed and incompetent.
30	1901	Wadsworth: J. Am. M. Asso., 1901, XXXVII, 1577.	M.	40 yrs.	Laborer.	"Stocky."		Apparently sudden.	
31	1901	MacFarland: *Ibid.*	M.	66 yrs.	Boxmaker.	Fairly well nourished.	About 16 mos.	Slow.	
32	1901	MacFarland: *Ibid.*	M.	56 yrs.	Laborer.	Emaciated.	About 6 wks.	Gradual.	Normal.
33	1901	Wier: See this report p. 43.	F.	36 yrs.	Housewife.	Well developed and well nourished.	About 4 yrs.	Comparatively slow.	Stenosed to 5 mm. i diameter, firm, o funnel shape and insufficient.
34	1910	Bunting: See this report, p. 53.	F.	29 yrs.	Housewife.	Stout.	Over 6 mos.	Slow.	Extremely contracte and appears as buttonhole sli which will not admit the little finge
35	1910	Rusk: State Hosp. Bull., Utica, N. Y., March, 1910.							

Character of Free-Thrombus.							Signs of Former Attachment.	Remarks.
Form.	Size.	Weight.	Surface.	Consistency.	Situation.	Section.		
ll.	3.5 cm. in diameter.	25 grams.	Finely warty and smooth.	Doughy.	Left auricle.	Concentric grey-brown-red layers with more homogeneous center.	Present.	
al.	3.5 cm. long.		Roughened at one end.		Left auricle.		Present.	The funnel-shaped space leading to the mitral orifice is here also noted. Osler believes it highly probable that the patient died of embolism of the left auriculo-ventricular orifice. The picture mentioned in the report does not exist (personal comunication, Mr. Broedel).
al.	3.5 x 2.2 x 2.2 cm.	8.5 grams.	Roughened on one side, smooth and shiny on one side.	Firm.	Left auricle.		Present.	One surface was flattened and roughened; the other round and smooth. It had evidently been free only a very short time.
ghtly al.	2 inches in diameter.		Smooth	Firm but elastic.	Left auricle.	Apparently laminated on periphery; soft center.		
	Large				Left auricle.			
	Soup bean.			Dense and firm.	Right ventricle.			This is evidently not a case of ball thrombus in the accepted sense of that term.
otely und.	3.5 cm. in diameter.	9 grams.	Everywhere perfectly smooth; stippled in appearance.	About that of congealed agar.	Left auricle.	Laminated periphery enclosing an irregular solid central mass.	None on the thrombus. Small adherent thrombus in auricular appendix.	
ticular.	3 x 2 x 1.5 cm.		Comparatively smooth, striated.		Left auricle.	Appearance laminated.		
					Left ventricle, aneurysmal dilatation.			

Age.—In 22 of the cases the age is given. This is found to vary from 2 to 66 years. Enumerated according to decades we have the following:

2—10, 1
10—20, 1
20—30, 9
30—40, 3
40—50, 6
50—60, 1

Occupation.—In 12 of the cases the occupation is given. These are as follows: Tailor, 1; servant, 2; laborer, 2; teacher, 1; book-binder, 1; box-maker, 1, and housewife, 2.

CLINICAL OBSERVATIONS.

State of Nutrition.—In 16 of the cases the state of nutrition of the patients at the time they were first seen is given. Of these 6 were poorly nourished or emaciated, 10 were fairly well nourished.

Previous Diseases.—In most of the cases these are too meagerly stated to be of value. However, so far as they are stated, they are as follows: Hemiplegia, 2; rheumatism, 3; influenza, 1, and scarlet fever, 1.

Initial Symptoms.—In all of the 20 cases, of which there is recorded a more or less complete clinical history, dyspnœa and palpitation of the heart were the most prominent symptoms first noted; in two of the cases it is not definitely stated.

Associated Conditions.—In eight of the cases there was a palpable thrill with a pre-systolic and a systolic murmur over the region of the left side of the heart accompanied by increase in the area of cardiac dullness and accentuation of the second pulmonic. In eight of the cases marked edema of the legs developed; in 3, circumscribed gangrene.

Clinical Diagnosis.—This is stated, or there is sufficient data in the account of 16 of the cases for it to be determined. They are as follows:

Dysentery	1
Pulmonary embolism	1
Mitral stenosis and insufficiency	4
Mitral stenosis and thrombosis of left auricle	1
Mitral stenosis	1
Mitral insufficiency	3
Malignant endocarditis	1
Cardiac insufficiency	4
Scarlet fever	1
Pulmonary tuberculosis	1
Croupous pneumonia	1
Acute appendicitis	1
Pseudocyesis	1

Character of Exitus.—In 21 of the cases the manner of death is stated or can be determined from the data given. They appear to be almost evenly divided, 11 having been slow and 10 sudden.

Post Mortem Findings.—There are fairly complete records of the observations made at autopsy in 24 of the cases. The following are the most important:

Pleural effusion	5
Pneumothorax	1
Chronic adhesive pleurisy	2
Infarcts of the lungs	3
Hydro-pericardium	3
Complete adhesion of the pericardium	2
Cardiac dilatation	17
Chronic endocarditis	18
Acute vegetative endocarditis on a chronic endocartitis	3
Thrombosis of the left auricle	14
Thrombosis of the right auricle	2
Infarcts in the spleen	4
Infarcts in the kidney	5
Chronic nephritis	3
Colloid goitre	1
Persistent thymus	1
Ulceration of the intestine	1

Condition of the Mitral Valve.—The condition of the mitral valve is stated in 29 of the cases. Of these 26 are mentioned as having been stenosed; in a majority of instances, to an extremely marked degree.

Form of the Thrombus.—The form of the thrombus is stated in 29 of the cases. They are as follows: Round, 19; oval, 5; lenticular, 1; cylindrical, 1; fusiform, 1; irregular, 2.

Size of the Thrombus.—The size of the thrombus is stated in 27 of the cases. This is found to vary from 4 cm. in diameter to the size of a pea. The most common size appears to be about 3.5 cm. in diameter.

Weight of the Thrombus.—In five of the cases the weight of the thrombus is given; they are over 4 grams, 9.55 grams, 25 grams, 8.5 grams, and 9 grams.

Surface of the Thrombus.—The character of the surface of the thrombus is stated or sufficient description is given so that its character can be inferred, in 20 cases. In 10 it is described as smooth; in 4, shaggy; however in all but six cases the thrombi were marked at one or more points by roughened areas. The endothelial covering noted by some of the authors, particularly by Krumbholz,* I believe to have been due to their interpreting the nuclei of leucocytes or desquamated endothelial cells, surrounded by interlacing strands of fibrin, arranged in parallel lines around the periphery of the thrombus, as flattened cells of an endothelial membrane. I herewith present a microphotograph (Fig. 16) taken from a portion of the periphery of the thrombus in my case which, to a certain extent, shows the condition I have mentioned above and how an error might occur.

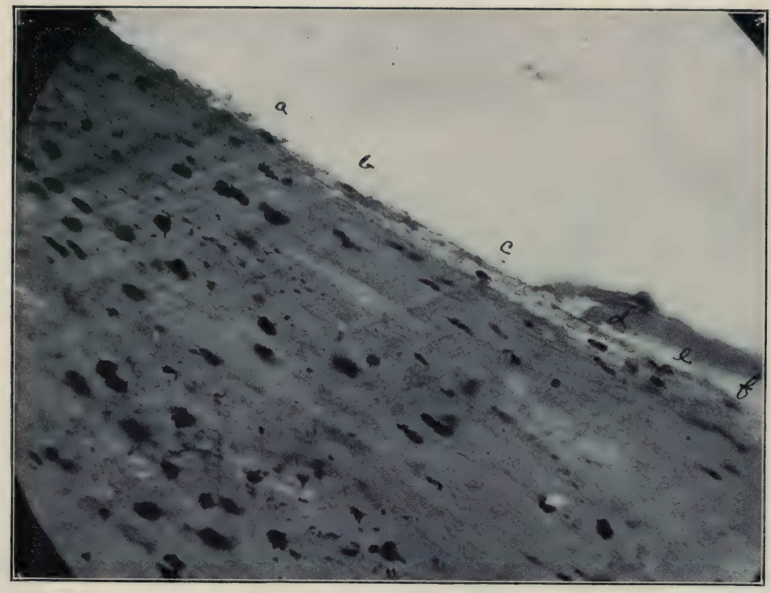

FIG. 16.—WIER'S CASE.

A microphotograph of the periphery of the thrombus, showing how the nuclei of leucocytes or desquamated endothelial cells surrounded by interlacing bands of fibrin might be interpreted as nuclei of the cells of an endothelial membrane surrounding the thrombus. The nuclei may be seen at *a*, *b*, *c*, *d*, *e*, and *f*.

Consistency of Thrombus.—The consistency of the thrombus is given in 19 cases. In 10 of the cases it was, apparently, firm; in nine, soft.

Situation of the Thrombus.—The situation of the thrombus is described in all of the cases. In 29 of the cases it was found at autopsy in the left auricle; in four, in the right auricle; in two, in the left ventricle.

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* *Loc. cit.*

Signs of Former Attachments.—In 16 cases we have statements concerning signs of former attachments. In 12 of the cases signs of former attachments were present either as roughened and ragged areas on the thrombus, or adherent mural thrombi, or both. In four of the cases no signs of former attachments were to be seen on the thrombus itself.

Number of Thrombi Present.—The number of thrombi found at post mortem is stated in 28 of the cases. In all but three of the cases it consisted of a single thrombus. In Wood's * case there were three free thrombi; in Legg's * first case, two; in Fürbringer's * case about 15 are mentioned as partly free and partly adherent.

FREE THROMBI.

Thus far I have considered all of the cases of so-called free thrombi reported in the literature and those cases I have been able to add. Evidently the facts as enumerated are not sufficient for any extensive generalization. One fact, I think, is certain, and that is, that authors have been too free in the use of the term free thrombi or ball-thrombi and that many of the cases so designated and described in the literature have no right to be so considered. However, they are there now, and anyone that reviews the subject will be called upon to consider them. Von Recklinhausen was the first to make any limitation to these cases. In his criticism of Macleod's case he points out that it lacked the first essential of having a free thrombus, viz., a thrombus of larger diameter than the orifice in front of it. He further argues that these thrombi, which in size compare to the diameter of the valve orifice in front of them as "a dwarf to a barn door," are essentially unsuitable for the study of free thrombi and should be altogether discarded, as he does Macleod's case; for there is no apparent reason why, if the thrombus was free at the moment, it was not swept along by the blood stream as an embolus.

Since none of the cases I have reviewed or presented have shown any signs or symptoms which can enable us to know, *intra vitam,* whether or when a free thrombus exists in the heart, and since polypoid and marantic thrombi may have a surface laminated and for the most part smooth and shining, it seems to me we can now go further in our limitation of these cases and say that before a loose thrombus found in the heart can be classed as a free thrombus, it must not only be larger than the orifice in front of it, but, also, it must possess a surface everywhere smooth and showing no signs of former attachment. Those that do show signs of former attachment can be classed only as probably free thrombi, the degree of probability, in a general consideration, being in direct proportion to the size of the roughened area on the surface which indicates where it was attached. It is unfortunate that the method of opening the heart *in situ,* as described by Virchow,[34] has generally been departed from. By the ordinary method [35] the heart is subject to great manipulation and undoubtedly heart thrombi that are attached to the heart wall by delicate fibrinous pedicles are readily broken off. Certainly, as noted by v. Recklinghausen,* it cannot be denied that such might be the case. It thus appears that in the formation of free thrombi in the cavities of the heart the hand of the prosector has most probably surpassed Nature.

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* *Loc. cit.*

However, that there are a few cases, where undoubtedly loose thrombi have existed in the heart for a long period before death, cannot be doubted.

BALL-THROMBI.

As stated before, the form of the thrombus is stated in 29 of the cases herewith reviewed. Of these 19 were round and five were oval. Of those mentioned as round thrombi, and concerning which a certain amount of clinical data is given, five (Wood, Legg's second, v. Rechlinghausen's two and Wier) were perfectly round and showed on their surface no signs of former attachment. Of the five oval thrombi one (Osler's first) was found perfectly free and there was no roughness on its surface to indicate a point of former attachment. These, so far as I have been able to determine, are the only cases in the literature of true and undoubtable ball- or oval thrombi. Several of the other 18 cases may have been free for a certain length of time before death, but it is also just as probable that they may have been attached polypoid thrombi and may have become detached during the manipulation of the heart at the post mortem examination. Also it is quite possible that, had the patient in many of the cases of probably loose thrombi lived longer, ball- or oval thrombi would eventually have been formed.

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* *Loc. cit.*

Mitral Stenosis and Insufficiency and Ball-Thrombi.—In all of the six cases mentioned above there was an extreme stenosis of the mitral valve and an accompanying marked insufficiency. On the existence of this condition undoubtedly depends, as noted by Wood, Ogle, Legg, v. Recklinghausen and several others, the formation of ball-thrombi.

One most interesting point in regard to them, as noted by Wood, is "how the circulation should have been sufficiently carried on to maintain life for any length of time." Another interesting question is why, out of the large number of cases of extreme mitral stenosis and insufficiency that have been autopsied, so few have shown free or ball-thrombi? The second question does not appear to have been mentioned before by any of the preceding writers on this subject; however, it seems to me to be worth considering.

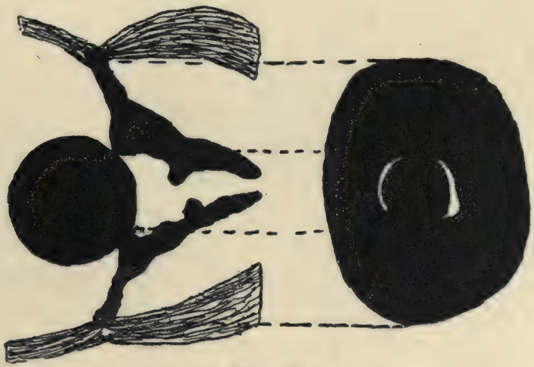

Fig. 17.

A schematic section and plan of a ball-thrombus and the mitral valve, showing how a round thrombus may not completely fill the opening in the top of the funnel shaped mitral orifice and an oval or an irregular shaped thrombus may. This further shows how, if the thrombus should become apposed over the valve orifice the weight of the thrombus and the inertia of the regurgitated blood would cause it to drop out at the first moment of ventricular systole.

Why do free and ball-thrombi not produce immediate death? That these thrombi may act as ball-valves was first argued by Legg. Hertz was the first to offer an explanation of how life continues in spite of this ball-valve action. He argued that the thrombus with each ventricular systole is thrown out of the orifice and remains out for the first part of the ventricular diastole, at least, so that sufficient blood passes from the auricle to the ventricle to maintain the circulation. Von Recklinghausen soon afterwards attacked this view, as well as other views of Hertz, on this subject. He argued that the orifice is oval and not round, so that a round body cannot possibly occlude the orifice completely unless it is pushed or wedged into it; moreover, the shape of the orifice is that of a shallow funnel, the walls of which are soft and, however the thrombus may fall, the conditions are such that the next moment it will roll out; besides, there is no arrangement for catching the ball or for holding it should it fall over the orifice. Lang, who had never seen a case, soon after this took up the discussion and advanced the idea that during the diastole of the ventricle, in consequence of the rigid base of the auricle and the great amount of grinding in its cavity, the horizontal pressure of the auricle was used up, for the most part, and, consequently, a part of the free content of the auricle, together with the weighty ball-thrombus, had to remain behind. Arnold in his report of a case of free thrombus emphasized this view of Lang and pointed out that a horizontal pressure can make itself of value on a clot only when it is lying in the orifice.

These points are all well taken and worthy of consideration. However, there are certain other points, I believe, that may be derived from a study of the anatomy and physiology of the heart that may aid in a solution of this question. In a normal heart, if one looks at the cavity of the left auricle, opened *in situ,* as at an autopsy, it can be readily seen that from the most dependent portion of the left auricle through the centre of the mitral orifice is an inclined plane, pointing forward and upward. This is true when the body is in the prone position. In the erect position this plane has apparently, also, an inclination forward and upward; moreover, a longitudinal section through the auricle and ventricle shows that the floors of the two cavities are as fossæ with the valve opening between them above the level of the lowest portion of either. With a markedly contracted orifice it is readily conceivable that the fossæ are much deeper. I, herewith, reproduce the thoracic portion of a schematic section through the median line of the human body (Figs. 18, 19). While this does not give the exact relations of the cavities of the left auricle and ventricle to each other, it nevertheless serves to illustrate the point which I have mentioned. Physiologically, on observing the mammalian heart beat in the opened chest, it is seen that the atrium of the auricle is never completely emptied,[36] a fair quantity of blood remaining over after each systole. It seems to me quite probable that this same condition exists in the human heart. With an extreme mitral stenosis, such as has existed in all of the genuine cases of ball-thrombus and in a majority of the cases of probably free thrombi, there is a marked stasis of blood and a consequent dilatation of the auricle. This, of course, deepens the atrial fossa and elevates the opening of the valve orifice still higher above the floor of the atrium. Accordingly, it appears to me, that when a clot of blood becomes loosened in the left auricle and there is the associated condition of extreme mitral stenosis, from its weight, it must drop and lie on the floor of the atrium. The floor of the atrium, being below the opening of the valve orifice, and the plane connecting the two being that of a curve or incline, with each auricular systole the force of the vertical pressure tends to drive the clot up this curved or inclined plane and toward the valve orifice, that of the horizontal pressure to raise it to the level of the plane of

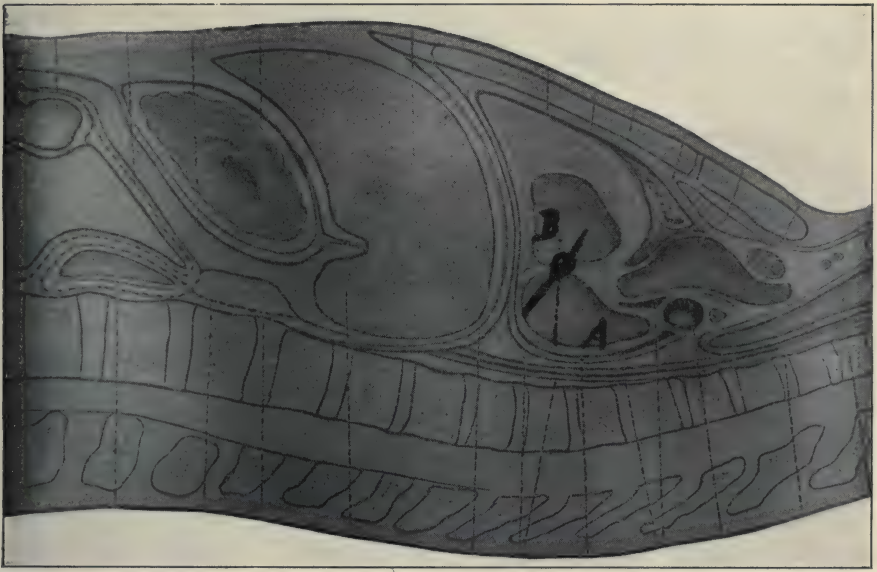

Fig. 18.

Schematic section through the median line of the body; *A* auricle, *B* ventricle, *O* stenosed mitral orifice; showing that in the reclining position, from the most dependent portion of the auricular atrium to the center of a stenosed and contracted mitral valve is an inclined plane.

the center of the valve orifice. As the atrium is not completely emptied in the normal heart, it is much less so in a heart with loss of compensation. It is thus conceivable that the force of the auricular contraction and the suction of the blood through the contracted valve orifice is not sufficient to raise a thrombus of 10 grams weight up to the level of the orifice, and it is thus never brought directly over it. Again it is conceivable that, should the thrombus become directly

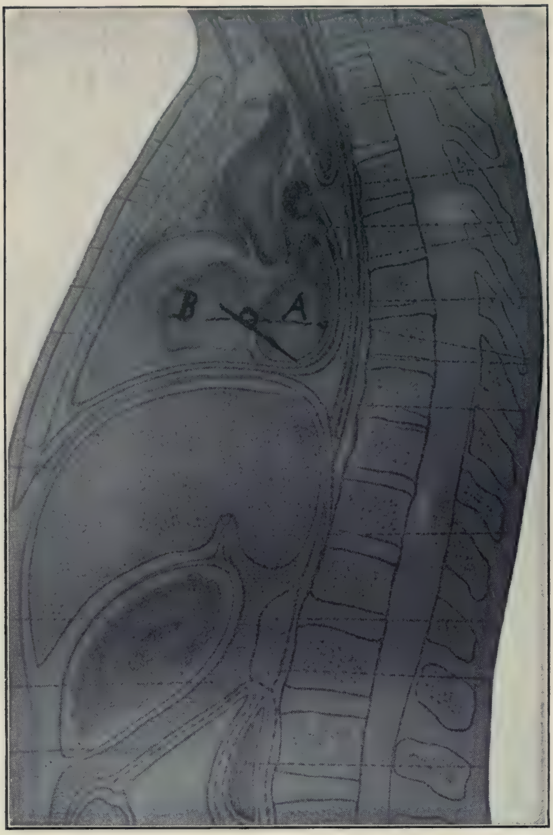

Fig. 19.

Same as Figure 18, in the erect position; *A* auricle, *B* ventricle, *O* stenosed mitral orifice; showing that in this position also from the most dependent portion of the atrium of the auricle to the center of the contracted mitral orifice is an inclined plane.

apposed over the orifice, the inertia of its weight and the fact (as mentioned by v. Recklinghausen and as is evident to any one who has seen a genuiue case) that the projections and prominences around the margin of the funnel-shaped and oval orifice are such as to preclude a complete obstruction of the passage (Fig. 17), would be sufficient to prevent its being drawn into the orifice, and at the first moment of auricular systole it would drop back on the floor of the atrium. It should be noted also that the force of the auricular systole normally, and more so in cases of great dilatation, is far less than that of the ventricular systole; the force of the ventricular diastole is normally less than that of the systole. Thus, the forces tending to drive the thrombus to the valve orifice are less than those tending to drive it away from the orifice. By force I mean the power or ability of the contracting auricle and ventricle and flowing blood to move an inert body.

Can a ball-thrombus cause sudden death? This question involves the ball-valve action of ball-thrombi and the opinions of the different authors on this point have already been referred to. Assuming all of the cases of free thrombi that I have collated to be genuine, the numerical relation between the cases of sudden and those of slow death in them is that of 10 to 11. Of the six genuine cases of ball- and oval thrombus that I have here mentioned the character of the exitus can be determined in only four. Of these only one died suddenly and that was the patient reported by Osler. Of the 11 cases of loose thrombus found in the heart associated with slow death in seven of them the shape of the thrombus is stated; four were spherical, three irregular or oval. Of the 10 cases of sudden death the shape of the thrombus can be determined in all; three were spherical and seven irregular or oval. These figures correspond with the observation of Welch "that an oval (or irregular) thrombus is more likely to plug the mitral orifice than a round one," assuming the thrombus to have been the cause of death. It thus appears that the evidence is that no case of genuine ball-thrombus, in contradistinction to the oval thrombus, has so far been reported in association with sudden death, nor is there any evidence that it occluded the mitral orifice. It appears, moreover, that the more nearly round the thrombus is the better are the chances that such an occlusion will not take place. However that a perfectly round thrombus may not produce an occlusion of the mitral orifice cannot be said.

Why are so few cases of marked mitral stenosis and insufficiency associated with ball-thrombi? As v. Recklinghausen has mentioned, sudden death in cases of extreme mitral stenosis is not very uncommon, and many of these cases may be due to a loose or ball-thrombus. However, until shown otherwise, we must accept the cases as reported from autopsy findings as representing, in a general way, the relation between loose thrombi and ball-thrombi, and mitral stenosis. It is, moreover, noticeable that more of the cases of mitral stenosis and insufficiency show, at section, mural thrombi than polypoid thrombi. As to why this should be, we can only conjecture. In these cases, at the time of broken compensation, and for a certain time before, both of the cavities of the auricle, the auricular appendix and the atrium, are greatly distended and recesses are formed from the main median passage of the atrium. Reasoning by analogy from the action of fluids in general flowing along passages with irregular walls, it is conceivable that in both these recesses there is more or less of a whirlpool-like rotation of the blood. In the smaller recesses, as between the musculi pectinati and in the tip of the auricular appendix, there may be practically stasis. It is here (for reasons that we will not discuss further than to say that it is most natural from the ease with which the thrombus can attach and hold itself to these muscle bands) that the marantic thrombi form and are generally found. The thrombus, once started, steadily grows toward the ostium of the appendix. Polypoid thrombi always project from the ostium of the auricular appendix. It is this projecting of the marantic thrombus from the ostium, in the first place, that gives rise to its becoming polypoid. The thrombus, having grown by slow accumulation of fibrin on its surface through the ostium to the margin of the main median passage of the atrium of the auricle where the blood flows for the pulmonary veins directly through the contracted mitral orifice, accumulates fibrin on its projecting end faster than at its attached base. Whether this polypoid thrombus will be round or oval or easily detached, will depend on the nature of the original projecting thrombus; if this is blunt with a pyramidal base the chances are that the polypoid thrombus will be oval and of a large size; if it is slender, it will probably be round and of a small size. A picture (Fig. 20: from Adami's Pathology[37]) shows a thrombus originating in the left auricular appendix and increasing in size until it has reached the mitral orifice. It is there mentioned "if its pedicle of attachment in the appendix becomes broken across, the liberated main mass would form a ball-thrombus." From what I have said before it appears to me that it would have more probably been an oval thrombus; but the most interesting question is, why did its pedicle of attachment not break across? The only obvious reason that I can think of is that the patient did not live long enough for sufficient fibrin to accumulate on the projecting end of the thrombus. The weight of the thrombus, together with the back and forth motions of the blood, must have eventually broken the thrombus loose. Then the processes of the rounding and smoothing of its surface would have

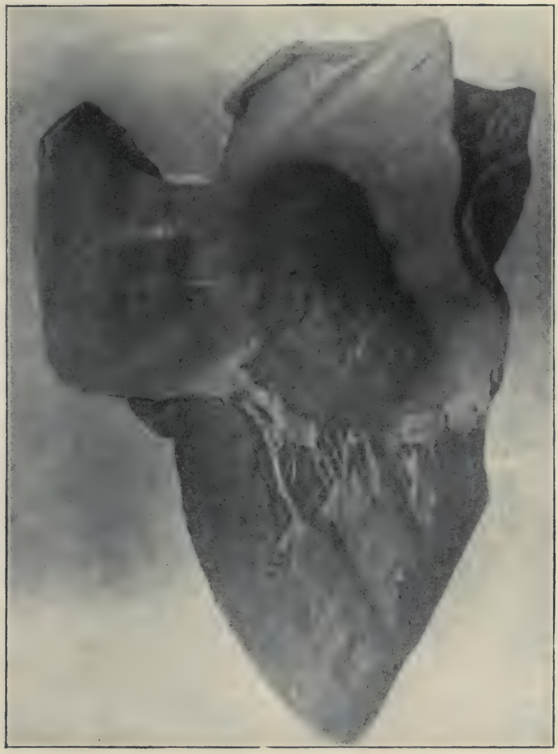

Fig. 20.

A thrombus from a case of Dr. Adami that had originated in the auricular appendix and increased in size till it reached the mitral orifice. It is readily conceivable that, had a marked mitral stenosis existed in this case and had the patient lived long enough, a ball- or oval thrombus might have formed.

begun until finally a perfect spheroid or ovoid of fibrin was formed. This, at present, seems to me the best explanation I can offer of why so few cases of mitral stenosis with insufficiency are accompanied by ball-thrombi. The process of their formation requires such a sequence of events and such length of time that some intercurrent infection kills the majority of patients before such an event can occur. It thus appears to me as probable that a ball- or oval thrombus may be associated with every case of extreme mitral stenosis with insufficiency in which the patient lives long enough for nature to do the work; and, conversely, every case of extreme mitral stenosis with insufficiency of sufficient duration may be accompanied by a ball- or oval thrombus.

Diagnosis.—Let not the internist be weary in well doing, there are laurels yet to be won in Internal Medicine. Never has a case of ball- or loose thrombus been diagnosed save in the post mortem room. From what has been heretofore presented, it is evident that no clinical difference can be made between ball- and loose thrombi and autochthonous thrombi, in general, when associated with marked mitral stenosis. As v. Recklinghausen and others have noted, no symptoms or signs have so far been elicited in a case of extreme mitral stenosis with ball- or loose thrombus that might not have occurred in a case of simple mitral stenosis of high grade. In fact, after almost a century, we are still unable to say anything more definite on this point than Wood said in the beginning: "All the symptoms of the disease, as well as the morbid appearances of the cavities of the heart, may be satisfactorily explained on the principle of obstruction to the free passage of the blood through the left side of that organ." Accordingly, in every case of marked mitral stenosis of long duration, loose or ball- or oval thrombi should be thought of. Their ultimate diagnosis must, until we have delicate methods of examining the heart and more data, be left to the post mortem room. It seems to me quite possible that with the more delicate instruments, the electrocardiograph, the electrophonograph, the polygraph, the cardiosphygmograph, or some other instrument of this kind that may be subsequently devised, some means may be discovered by which the presence of thrombi in the heart may be detected.* By this means also the observations must be extended over a long period of time and be corrected by autopsy findings, so that we are still not much nearer the end.

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* For an excellent summary of practically all the work that has been done along this line the reader is referred to two comparatively recent papers by Dr. Lewellys F. Barker.[38] [39]

Treatment.—Here nothing can be said that may not be found in any of our recent and recognized text books on medicine in the chapter on the treatment of mitral stenosis and insufficiency. It may not be out of place here to point out that, if the relation of the ball- or loose thrombus to the atrial fossæ is as I have indicated, absolute rest of the patient in a supine position is very necessary and that the patient should not be allowed to get up or even to assume a sitting posture. It seems possible that in Stange's and Lohlein's and other cases, here reviewed, life was shortened by the patient not observing this precaution. However, in Löhlein's case there was a preceding attack while lying in bed, and in Osler's second case sudden death ensued with the patient at rest and in bed. Of course, in the light of our present knowledge of this condition, strictly followed, such treatment would mean the confinement of all cases of marked mitral stenosis with insufficiency of long standing in a supine position for life and with no other end to be attained than the prolongation of the life of the individual for a variable period—a practice that would appeal neither to physician nor patient.

Conclusion.—In conclusion I think it can be safely said:

1. Thrombi found on post mortem examinations loose and free in the cavities of the heart should not be classed as such, unless all possible chances of their having been loosened during the examination can be excluded, or there are on their surface no signs of former attachment to the auricular wall.

2. The term ball- or oval thrombus of the heart should be restricted to those thrombi, found on post mortem examinations loose in the heart cavities, which are of a round or oval shape and whose surface is everywhere smooth and shows no signs of former attachment.

3. Those thrombi found on post mortem examination loose and free in the cavities of the heart which do show signs of former attachment and the possibility of their having been loosened during the post mortem examination cannot be excluded, should be classed as probably loose or free thrombi; the degree of probability varying with the size of the roughened area of attachment, the distance of the thrombus from its points of attachment, the size of the valve orifice in front of it, etc.

4. Those small thrombi, found loose in the cavities of the heart on post mortem examinations, which are in front of a valve orifice many times their diameter in size, should not be considered among loose or free thrombi at all.

5. To William Wood, of Edinburgh, belongs the honor of describing the first case of genuine ball-thrombus of the heart.

6. The origin and formation of ball-thrombi of the heart is dependent on an obstruction to the free passage of blood by a narrowed and constricted valvular orifice of the heart.

7. All cases of genuine ball- or oval thrombi of the heart, thus far reported, have been found in the left auricle and have been associated with marked mitral stenosis and insufficiency.

8. That genuine ball-thrombi in the heart may act as ball-valves appears possible, but has yet to be definitely demonstrated.

9. That oval or irregular, and recently detached thrombi may produce sudden occlusion of the auriculo-ventricular orifice appears more probable and very possible.

10. No sign or symptom has so far been described that will enable one to diagnose definitely autochthonous thrombosis, loose thrombi, or ball- or oval thrombi in a case of marked mitral stenosis with insufficiency; consequently no practical treatment different from that ordinarily employed in mitral stenosis with insufficiency can be recommended.

I desire to express my thanks to Dr. W. T. Howard, of the Western Reserve Medical School, Cleveland (Ohio), and to Dr. F. F. Wesbrook, of the University of Minnesota, for aid and suggestions in the preparation of this paper; to Mr. J. T. Gerould and Mrs. F. M. Leversee, Librarians of the University of Minnesota and its Pathological Department, respectively, for securing reference books for me and for aid in the preparation of the manuscript; also to Mr. Henry Andrews, of the photographic department, University of Minnesota, for most of the accompanying photographs; and to the various men who have kindly sent me reports of their cases.

St. Joseph's Hospital.

REFERENCES.

1. OSLER: J. Anat. & Physiol., 1879-80, XIV, 230.
2. WOOD: Edinb. M. & S. J., 1814, X, 50.
3. CADY: Boston M. & S. J., 1856, LIII, 477.

4. Van der Byl: Trans. Path. Soc., London, 1858, IX, 89.
5. Ogle: *Ibid.,* 1863, XIV, 127.
6. Legg: *Ibid.,* 1878, XXIX, 49.
7. Macleod: Edinb. M. J., 1882-3, XXVIII, 696.
8. v. Recklinghausen: Handb. d. allg. Path. d. Kreislaufs u. d. Ernährung, Stuttgart, 1893, and Deutsches Arch. f. klin. Med., 1885, XXXVII, 495.
9. Hertz: Deutsches Arch. f. klin. Med., 1885, XXXVII, 74.
10. Welch: Allbutt's System of Medicine, 1899, VI, 185.
11. Lang: Wien. med. Presse, 1886, XXVII, 209.
12. Osler: Montreal M. J., 1897, XXV, 729.
13. Arnold: Ziegler's Beitr. f. path. Anat. u. f. allg. Path., 1880, VII, 29.
14. Fürbringer: Deutsche med. Wchnschr., 1890, XVI, 505.
15. v. Ziemssen: Congress f. inn. Med., 1890, 281.
16. zum Busch: Ueb. d. Zusammensetzung d. Herzthromben. Inaug-Diss. Freiburg, i. B., 1891.
17. Schmorl: Schmidt's Jahrbücher d. in- und ausländischen gesamten Medezin, 1892, CXXXV, 110, and Stereo-scopish-photographer Atlas d. path. Anat. d. Herz. u. d. grosseren Blutgefässe, München, 1899, Tafel 20.
18. Redtenbacher: Wien. klin. Wchnschr., 1892, V, 688.
19. Lang: Wien. klin. Wchnschr., 1892, V, 618.
20. Rosenbach: Die Krankheiten d. Herzens, 1893, I, 180.
21. Krumbholz: Arb. a. d. med. Klin. zu. Leipzig, 1893, 328.
22. Stange: Arb. a. d. path. Inst. zu. Göttingen, 1893, 232.
23. Zchu: Internat. Beit. zur wissensch. Med., Virchow's Festschrift, II, 199.
24. Aschoff: Virchow's Arch., 1892, LV, 93.
25. Bostroem: Deutsches Arch. f. klin. Med., 1895, LV, 219.
26. Eichorst: Pathologie u. Therapie, Zurich, 1895, 121.
27. Tauber: Jahrbuch d. Wiener k. k. Kranken-Anstalten, 1896, V, 345 (Wien. u. Leipzig, 1898).
28. Osler: Johns Hopkins Hosp. Rep., 1891, II, 56.
29. Löhlein: Inaugural Dissertation, Univ. of Giessen, 1900.
30. Wadsworth: J. Am. M. Asso., 1901, XXXVI, 1577.
31. McFarland: *Ibid.*
   ——— Text-Book of Pathology, 1910.
   ——— *Ibid.,* 113.

32. Ernst: Cor. Bl. f. schweiz. Aerzte, 1905, XXXV, 16.
33. Rusk: State Hosp. Bull., Utica, N. Y., March, 1910.
34. Virchow: Post Mortem Examinations, translated by T. P. Smith, M. D., Philadelphia, 1891, 47.
35. Mallory and Wright: Pathological Technique, fourth edition, 1908, 33.
36. Howell: Text-book of Physiology, 1910, 521.
37. Adami and Nicholls: Principles of Pathology, 1909, II, 62.
38. Barker: Johns Hopkins Hosp. Bull., 1909, XX, 297.
39. Barker: *Ibid.,* XXI, 358.

BENZOL AS A LEUCOTOXIN.*

STUDIES ON THE DEGENERATION AND REGENERATION OF THE BLOOD AND HÆMATOPOIETIC ORGANS.†

By LAURENCE SELLING, M. D.

(*From the Pathological Laboratory of the Johns Hopkins University.*)

Benzene, or benzol, C_6H_6, is a product of the fractional distillation of coal tar. As employed in commerce, the term benzol is used to indicate a more or less impure material, containing in addition to C_6H_6, variable quantities of toluol, xylol and small percentages of carbon disulphide, thiophene, etc. It is to be distinguished from benzine, which is a product not of coal tar, but of crude petroleum, and which is composed chiefly of hexane and heptane.

A study of clinical material ‡ has shown that benzol (C_6H_6) is a powerful leucotoxic agent, producing destruction of the white cells of

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* This paper was published originally in German in Ziegler's Beiträge zur pathologischen Anatomie und zur allgemeinem Pathologie, 1911, 21, 556. It is reprinted with the kind permission of the editor Dr. L. Aschoff. The publishing house of Gustav Fischer in Jena has supplied the illustrations.

† Aided by a grant from the Rockefeller Institute for Medical Research.

‡ The work to be reported was suggested by a series of cases which occurred in the service of Dr. L. F. Barker, at the Johns Hopkins Hospital, in 1909. The clinical and pathological discussion of the cases has been made the subject of a report in the Bulletin of the Johns Hopkins Hospital,[46] but it may be well to summarize briefly the chief facts of interest.

The patients, three in number, were girls fourteen years of age, all employed in one room of a factory for the manufacture of tin cans. In this room a special type of can was made, in which rubber was used as a substitute for solder. The pure rubber, along with an earthy coloring matter and a rosin, were dissolved in commercial benzol, and subsequent experiments demonstrated that the benzol (and more particularly the benzene (C_6H_6) fraction of the benzol), was responsible for the poisonings. The results were the same whether the impure commercial product or the chemically pure product (C_6H_6) was used. The chief absorption of the toxic material was through the lungs.

Two of the three cases admitted to the hospital terminated fatally. These patients had been working in the factory for four to five months, and noted the first symptoms about one month before admission. The chief clinical features were:

the circulating blood, and severe injury to the bone marrow. As a result of experimental work it has been found that the effect of the poison is not confined to the circulating blood and the bone marrow, but that it involves the entire hæmatopoietic system—bone marrow, lymph glands, spleen and lymphadenoid tissue of the intestine. These organs are all affected, and the changes are similar in kind, but, as will be seen, there are differences in the degree of the injury. Myeloid tissue is more injured than lymphadenoid tissue, and correspondingly the polynuclear elements of the blood are more involved than the non-granular mononuclear elements. The nucleated red cells of the marrow are destroyed, but the circulating erythrocytes are relatively little affected.

The present paper is an experimental study of benzol poisoning with especial reference to:

(1) The course and extent of the degenerative changes in the white cells of the circulating blood and the parenchyma cells of the hæmatopoietic organs.

(2) The extent of injury after which the hæmotopoietic organs are capable of complete recovery.

I. *Purpura hæmorrhagica*, with typical skin lesions, with bleeding from the mucous membranes, and retinal hæmorrhages.

II. *Blood picture*, which was in general that of an aplastic anæmia.

(a) *Leucopenia.* This was the most striking feature of the blood examination. One case entered with a leucocyte count of 1280 cells per cmm., which dropped to 480-600 cells per cmm. before death. The other case entered with a count of 560 cells per cmm., which dropped to 140 cells per cmm. before death.

(b) Relative decrease in the polymorphonuclear elements, 43% and 18% respectively, and relative increase in the mononuclear non-granular elements, 55% and 81% respectively.

(c) *Anæmia.* In one case this reached 640,000 red blood cells per cmm., in the other 1,150,000. The corresponding hæmoglobin values (Sahli) were 8% and 15%.

(d) Only slight changes in the appearance of the red blood cells. Slight anisocytosis and pallor; no poikilocytosis.

(e) Scantiness of blood platelets.

(f) Absence of regenerative forms. No myelocytes and only one nucleated red cell (a megaloblast) were found.

The patients seemed in fairly good condition on admission, but showed a steady downward course, with symptoms of severe toxæmia (high fever, rapid pulse, dulness), with increase in the purpura, and with a progressively increasing anæmia and leucopenia. Death occurred six to seven days after admission.

(3) The course of the regenerative changes.

The study of the regenerative changes in the spleen has brought out additional points of interest in regard to

(a) myeloid metaplasia.

(b) The conversion of the erythroblast to the erythrocyte, by the extrusion of the nucleus.

I. LITERATURE.

A. BLOOD.

It is not our purpose to discuss in detail the extensive modern literature on the blood, but merely to give a brief summary of those facts and theories which are of importance for the work which follows:

(a) *Development of Blood Cells.*—With regard to the origin of blood cells, there are in general two theories held, the monophyletic and the polyphyletic. The supporters of the monophyletic theory consider that all the cells of the blood and hæmatopoietic organs have a common parent cell, either the large lymphocyte (Maximow,[30] [31] Saxer,[45] Dominici,[18] Pappenheim[42]) or a still less differentiated and somewhat hypothetical lymphoid cell (Wolff[56]). The supporters of the polyphyletic theory consider that there are separate parent cells for the different cell types, but the different authors disagree both as regards the number of parent cells, and the cell groups derived from each. The majority, however, believe that there are two parent cells (Ehrlich,[14] Naegeli,[38] Schridde[46]) from the one are derived the cells of the myeloid series—granulocytes, erythroblasts and megacaryocytes—and from the other are derived the cells of lymphatic series.

Schridde,[47] by a modification of the Altmann method, found that the large lymphocyte—the chief element of the *Keimcentra* of the lymph glands—could be sharply differentiated from the myeloblast—the cell of origin of the granulocytes—by a specific granulation in its protoplasm, and thus offered new ground for the acceptance of the polyphyletic theory. His work is accepted by Naegeli,[38] who considers that the granulocytes and lymphocytes are of different origin, not only because of this difference in the granulation of the parent cell, but also because of differences in the biological reactions. Otherwise, however, Schridde's findings have met with very general skepticism (Butterfield, Meyer, Heinecke,[6] Maximow,[33] Weidenreich, etc.).

The monophyletic theory has been greatly strengthened by the recent studies of Maximow[30] [31] [33] on the rabbit, and Dantschakoff[9] [10] on the chick. Both these observers, following the embryonic development from the earliest stages, find that the common parent cell of the blood, along with the endothelium of the primitive blood vessels, is derived from the mesenchymal elements. This parent cell is identical with the large lymphocyte of later life. At first it differentiates almost entirely in the direction of the primitive erythroblastic elements. From the large lymphocytes, and from the mesenchymal cells direct, primary wandering cells form throughout the tissues. After the formation of primitive erythroblasts is well advanced, these wandering cells begin to differentiate into first, definitive erythroblasts, and later, granulocytes. The definitive erythroblasts develop in the form of circumscribed islands, throughout the mesenchyme. Later granulocytes appear, usually separate from the erythroblastic islands, and for the most part as isolated exemplars. The lymphocytes, as do these other cell types, arise from primary wandering cells.

This work confirms in many respects, the earlier work of Saxer.[45] This author, studying somewhat more advanced embryonic stages, found that the primitive wandering cells give rise to all the cells of the blood and hæmatopoietic organs. The nucleated red cells arise in the form of definite cell islands through the connective tissue, the granulocytes either singly or in cell groups. The granulocytic and erythroblastic foci are separate from each other.

This development of blood cells in the form of groups or islands has been noted not only in embryonic life, but also in post-embryonic life. Maximow[30] in a study of the development of bone and bone marrow in the kidney, after ligation of the large blood vessels at the hilus, finds that, as the myeloid tissue develops in the marrow cavity, the granulocytes and erythroblasts do not occur in a confused mass, but as separate islands and groups. Weidenreich[55] (p. 395), says: "Während in einzelnen Blutnestern allerdings rote und weisse Blutkörperchen in allen Entwickelungsphasen übereinander getroffen werden, bieten doch sehr viele ein einheitlicheres Bild, so dass sich Gruppen der roten und weissen Entwickelungsreihen häufig voneinander getrennt festhalten lassen."

Bunting,[4 5] working with ricin and saponin, both of which produce severe injury to the bone marrow, states: "That conception was obtained that the red marrow of the rabbit normally consists essentially of a patchwork of cells arranged in groups or proliferating centers; certain groups composed of indifferent myeloblasts . . . . surrounded by myelocytes and . . . . mature polynuclear cells; others composed of immature red cells or even indifferent myeloblasts . . . . with surrounding layers of megaloblasts, intermediates and normoblasts, and peripheral layers of mature red cells.

(b) *Regeneration of the Bone Marrow.*—During the later embryonic development, the bone marrow contains very large numbers of elements of the youngest types, 60-70% myeloblasts (Naegeli) and many megaloblasts. As development proceeds the proportion of these younger elements becomes progressively less, and throughout adult life, under normal conditions, the predominating cells in the marrow are myelocytes, polymorphonuclear leucocytes and normoblasts. The cell content of the marrow is kept up by the constant proliferation of the more differentiated cells. When additional call is made for increased cellular reproduction, they are the ones which respond (Türk[55]). The hyperplastic marrow of pneumonia and that following severe hæmorrhage furnish examples of this type of proliferation.

In pernicious anæmia conditions are different. Here, whether because of more severe injury to the marrow, or more prolonged demands made upon it, or both, there is reversion to the embryonic type, and there is again a great increase in the number of myeloblasts and megaloblasts. In some of these cases of pernicious anæmia, for reasons that are not understood, the marrow may become exhausted, and entirely fail to respond to the demands made upon it—*i. e.*, the cases of aplastic anæmia. Hirschfeld[58] has reported a similar condition in a case of purpura hæmorrhagica. Blumenthal and Morawitz[8] succeeded in producing somewhat analogous conditions in animals by repeated bleedings over a long period of time.

These conditions of marrow exhaustion are relatively uncommon, for normally the bone marrow is possessed of remarkable regenerative and recuperative powers. In man we know that it is capable of compensating a great loss of blood cells. Experimentally, Heinecke[19] has shown that after the marrow has been rendered almost wholly aplastic by exposure to Roentgen rays, it can recover completely in a period of 3-4 weeks. In these experiments it was the younger bone marrow elements, the myeloblasts, which were the first to return.

In general the response of the marrow is not specific. It does not respond to a loss of white blood cells solely by the reproduction of granulocytes, nor to the loss of red blood cells solely by the production of erythroblasts. As Shridde[46] points out, the regeneration of the blood cells seems independent of the needs, and in the individual case it is hard to prophesy just what proportion of granulocytes and erythroblasts will be found. Blumenthal and Morawitz[3] explain this on the basis of an interrelation (*Wechselbeziehung*) between the two types of tissue.

(c) *Conversion of Erythroblasts and Erythrocytes.*—According to Kölliker[35] and Neumann,[40] [41] who were the first to discuss the problem, the conversion of the erythroblast to the erythrocyte takes place by an intracellular solution of the nucleus. Doubt was thrown on this view by the observation of Rindfleisch,[48] who noticed that in fresh blood to which 0.6% sodium chloride solution had been added the nucleus was extruded from the cell body. Since Rindfleisch, the various investigators working in this field, have adopted one or the other of the two theories, or have taken the middle stand, that both methods occur physiologically (Block[2]).

For those who hold the theory of intracellular degeneration of the nucleus, the process may represent either a gradual solution of the entire nucleus (caryolysis), or a fragmentation of the nucleus (caryorrhexis) followed by solution of the fragments. Israel and Pappenheim,[34] who accept this theory, consider that the pictures interpreted as demonstrating nuclear extrusion, are due to artificial causes—*e. g.*, the exertion of pressure in making cover slip preparations, or, in Rindfleisch's observation, the addition of 0.6% sodium chloride solution. They admit the presence of naked nuclei in small numbers, but explain them on the basis of degeneration of the protoplasm, leaving the nucleus free.

The authors who accept the extrusion theory, point to the presence of naked nuclei in the blood and hæmatopoietic organs, for which they cannot accept Israel and Pappenheim's explanation. They point to pictures, both in blood smears made with all care, and in sections of fixed tissue, in which the various stages of extrusion may be seen: a more and more eccentric position of the nucleus; partial extrusion, in which part of the nucleus lies within the cell, and part without; complete extrusion, in which the nucleus is found lying close to the cell from which it came. In order to overcome Israel and Pappenheim's objections, that the phenomena seen by Rindfleisch were artificially produced by the presence of the sodium chloride solution, Weidenreich[55] examined bone marrow cells in blood serum, and was enabled to confirm Rindfleisch's observation.

The pictures of caryolysis and caryorrhexis, which are interpreted by the upholders of the intracellular theory in support of their view, are explained by some of those who adhere strictly to the extrusion theory as the results of imperfect fixation. By most, however, they are admitted as physiological processes which precede extrusion. The nuclei which are extruded are not young healthy exemplars, but such as have undergone changes—pyknosis, shrinkage, caryorrhexis or partial caryolysis. Following fragmentation of the nucleus, the individual fragments may be extruded separately (Weidenreich[55]) and small portions may even remain in the cell body for some time.

Albrecht, whose view is accepted by Weidenreich, considers that extrusion takes place as a result of variations in surface tension between plasma and cell body, cell body and nucleus. Howell[23] suggests the possibility of a migration out of the nucleus; an active rather than a passive process.

A detailed discussion of the various theories and the literature may be found in the articles of Israel and Pappenheim,[24] Block[2] and Weidenreich.[55]

(d) *Myeloid Metaplasia of the Spleen.*—Myeloid metaplasia of the spleen, or the occurrence in the spleen of the various bone marrow elements—myelocytes, erythroblasts and megacaryocytes—has been described in recent years in a great variety of conditions: pernicious anæmia, and myeloid leukæmia; severe secondary anæmias both in man and in experimental animals; severe infectious diseases; tumors of the bone marrow and osteosclerosis, and of late, also in lymphatic leukæmia (Hirschfeld[21]).

At first the view prevailed that the occurrence of these elements in the spleen was dependent on the sweeping in and further development of unripe cells from the bone marrow. Doubt was thrown on this view by the occurrence of cases in which myeloid elements were found in the spleen without any corresponding elements in the circulating blood, and also by the finding of occasional similar cells in the normal spleen (Dominici,[12] [13] Sternberg,[50] Kurpjuweit). This led to the theory of the autochthonous development of the myeloid elements, whether from preexisting cells of the same type, or by further differentiation of a parent cell (*e. g.*, large lymphocyte) in the spleen pulp. The majority of the more recent writers have accepted the view of the autochthonous origin of the myeloid tissue in the spleen (Meyer and Heinecke,[34] [35] Morris,[37] Domarus,[11] Butterfield,[7] Schridde[46]); while others (Sternberg,[49] Morawitz and Rehn[36]) consider either method possible.

Meyer and Heinecke pointed out clearly the relation of the myeloid tissue to the lymphoid tissue, with regard to the distribution of the various elements. The myeloid tissue always develops in the red pulp (sinuses and cords) and not in the white pulp (Malpighian corpuscles). As it increases in amount, it encroaches on the Malpighian corpuscles causing a pressure atrophy. They, and also Domarus, consider that the changes in the spleen represent a reversion to the embryonic type—a resumption by the spleen of its embryonic function of hæmatopoiesis, the entire process being compensatory in nature.

Sternberg,[40] while accepting the possibility of autochthonous origin of the myeloid cells, thinks the sweeping in of bone marrow elements more probable, and associates the myeloid metaplasia rather with the function of the spleen as a blood filter, than with its function as a hæmatopoietic organ. In many cases, he finds the amount of myeloid tissue present too small to justify its being classified as a myeloid metaplasia, or to be of any value as a compensatory phenomenon.

B. BENZOL POISONING.

The great majority of reported cases are those in which relatively large doses of the poison have been received, either by mouth, or by inhalation. In these cases, whether terminating fatally or in recovery, the course has been acute and the symptoms referable chiefly to the central nervous system. Either there has been insufficient time for the development of the leucotoxic effect, or such changes, if present, have been overlooked.

In a series of cases reported by Santesson,[44] chronic poisoning by benzol—the impure, commercial product—resulted from repeated inhalations, and all these cases, as did our own, showed a very striking diminution of the white blood cell count.

The only other mention found in the literature as to the effect of benzol on the blood and hæmatopoietic organs, occurs in some experimental work by Langlois and Desbouis.[26 27] These observers found that the vapors of benzol and certain related hydrocarbons caused a distinct increase in the red cells of the circulating blood—an effect which they attributed to increased blood formation. The hyperglobulia disappeared two days after the cessation of inhalations. It was not constantly obtained when the drug was given by subcutaneous injection. They also found a slight diminution of the white blood cells, but attributed it to accidental causes.

C. EFFECT OF ROENTGEN RAYS ON THE BLOOD AND HÆMATOPOIETIC ORGANS.

Heinecke,[18] in a study of the effect of Roentgen rays on rabbits, guinea pigs and mice, found, as a result of the exposures, a marked leucotoxic, especially lymphotoxic action which shows many analogies to the effect of benzol injections.

The changes produced by X-rays, consist essentially in a destruction of lymphocytes. Examination of the lymph glands after a variable number of days shows the effect of the destructive action, in the almost complete absence of these cells. Both follicles and medullary cords are affected, the latter to a less marked degree. The lymph follicles of the intestine, and the Malpighian corpuscles of the spleen, show analogous changes.

*Splenic Pulp.**—Marked changes begin later than those in the lymph glands. They consist of a progressive cellular destruction, which requires for its production a greater intensity and duration of exposure. There is a moderate increase in the pigment content of the spleen, the increase being proportional to the duration of life after exposure.

In the lymphadenoid tissue and spleen pulp, the changes are less after 12-14 days than after 3-4 days, which the author refers to regenerative changes.

Bone Marrow.—Coincident with the changes in the lymphadenoid tissues, goes a destruction of the parenchyma of the bone marrow. This is less in degree than the changes in the lymphadenoid tissues, and even in the most advanced stages, representatives of all the cell types may be found. The small lymphocytes and large "non-granular myelocytes" (myeloblasts—large lymphocytes) suffer first. The neutrophiles, especially the neutrophile polynuclears are most resistant, and predominate throughout. After 2-2½ weeks regenerative processes begin, which are concluded in 3-4 weeks, with a restoration of the marrow to normal. The non-granular forms (small and large lymphocytes) regenerate first. During regeneration, as during degeneration, the polynuclear neutrophiles predominate. The nucleated red cells are destroyed along with the white cells of the marrow.

Blood.—After two or more days, according to the duration of exposure, the white blood count begins to fall. Qualitatively the lymphocytes are relatively reduced. Polynuclear elements and large mononuclears are scarcely affected. No abnormal blood cells are found. The predominance of polynuclears in the blood, corresponds with the fact that the lymphatic apparatus is more affected than the myeloid organs. The red blood cells show no change until the third week, when their number is a little reduced.

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* In Heinecke's first article[18] he considered the bone marrow along with the splenic pulp. Subsequent experiments[19] changed his conception and accordingly the bone marrow is considered separately below.

Helber and Linser[20] showed that the leucocytes were destroyed in the circulating blood by the effects of the X-rays.

II. Material and Methods.

Adult rabbits were used in most of the experiments. Attempts were first made to produce chronic poisoning by inhalation, but as these resulted unsuccessfully, recourse was had to subcutaneous injections. Commercially pure benzol, C_6H_6, mixed with equal parts of olive oil to render it less irritating, was injected under the skin of the abdomen with the usual aseptic precautions. As this produced considerable œdema over an area of 3-6 sq. cm., each subsequent injection was made in a different place. Absorption of the benzol-oil mixture was slow, and even after several days, on incision into the œdematous area, a marked odor of benzol was noted. In some cases, these areas became the seat of a chronic inflammatory process, which terminated in the production of a zone of dense induration.

The injections were given daily, the dose being 1 cc. per kilo of body weight. For convenience the experiments have been divided into three groups.

1. Descending series: Nine experiments, beginning with an animal killed twenty-fours hours after the first injection and ending with one killed twenty-four hours after the ninth injection.

2. Six experiments in which the animals received from five to ten doses, and died two to five days after the last injection.

3. Ascending series. Twelve experiments. Here the attempt was made to bring about an aplasia of the hæmatopoietic organs, especially of the bone marrow, after which regeneration was permitted to occur for variable periods of time. Considerable difficulty was encountered in obtaining this series. Owing to variations in the susceptibility of the animals to the drug, a uniform number of doses did not result in a similar degree of injury. It was found, however, that variations in the white blood count gave a fair index of the condition of the bone marrow, the count dropping as the aplasia became more marked. Using

the leucocyte count as a control, sufficient injections were given to lower the count to 200-800 cells per cmm. In this way a well-marked aplasia of the marrow was produced in most cases. If, after this point was reached, one or two additional injections were given, the result was usually fatal. The number of injections varied from four to nine.

As a control, red blood counts, white blood counts and blood smears were made daily on each animal for two or three days before the injections were begun. In many of the experiments these daily counts were continued throughout the course. The red blood counts for the normal animals varied from 4,500,000 to 7,120,000 cells per cmm.; and the white blood counts from 3000 to 11,680 per cmm. This corresponds to Gruber's[4] findings, in which the red cells for normal rabbits varied from 4,500,000 to 7,500,000 and the white cells from 5000 to 14,000 per cmm.

In general the normal counts remained fairly constant from day to day. This is especially true of the red blood cells, where variations of over 200,000 were uncommon. The white cells showed greater physiological variations, but where these were sufficiently great to interfere with the interpretation of the experiment, the animal was discarded, or the counts continued until they remained fairly constant for three successive days.

Autopsies were performed in most cases immediately after the death of the animal. Material for microscopic examination was fixed in Zenker acetic solution and stained with hæmatoxylin and eosin. Portions of the bone marrow (femur) were fixed in Zenker acetic and stained with hæmatoxylin and eosin, or with eosin-orange-toluidin (Dominici).* Other portions were fixed in corrosive sublimate alcohol, and stained with Giemsa solution, as described by Giemsa[16]; paraffin imbedding was used throughout. Bone-marrow smears, from femur and rib, were stained by Giemsa, hæmatoxylin and eosin, and methyl-green pyronin.

For the first two or three injections the animals generally remained in good condition. Then they became dull, and showed anorexia and loss of weight. In the advanced stages of the poisoning there were emaciation, more or less instability of gait, and tremors, terminating eventually in paralysis of the extremities, clonic and tonic convulsions, and death. Where the poisoning was not carried as far, recovery was complete.

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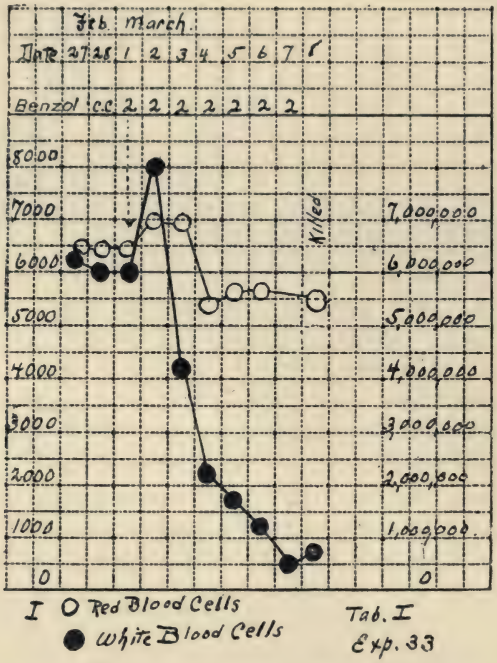
* See Maximow.[30]

III. CHANGES IN THE CIRCULATING BLOOD.

A. GENERAL.

The course of the changes in the blood is indicated in the charts given below. An example is taken from each of the three groups of experiments.



Exp. 33.—Series I. Adult rabbit. Weight 1940 grams. 2 cc. Benzol in an equal amount of olive oil injected daily for 9 days.

Exp. 37.—Series II. 2 cc. Benzol in an equal amount of olive oil injected daily for 6 days. Died 3 days after last injection.

Exp. 44.—Series III. Adult rabbit 1930 grams. 2 cc. Benzol in olive oil injected daily for 4 days. Killed 11 days after final injection.

The animal was in excellent condition throughout.

B. WHITE BLOOD CELLS. SERIES I (DESCENDING).

In two-thirds of the cases the white blood cells began to fall within 24 hours of the first injection, the drop varying from 80 to 6800 cells per cmm. with an average of 2200. In one-third of the cases there was an initial rise within the first 24 hours, varying from 240 to 2200 cells per cmm., with an average of 1160. In all cases, 24 hours after the second injection there had been a decided fall in the number of leucocytes. As the injections continued, there was a further drop from day to day, with only occasional breaks in the downward curve until, in the most severe case, no cells at all were found in the ruled portion of the counting chamber, and only an occasional one about the margin of the disk. (See Charts I and II.)

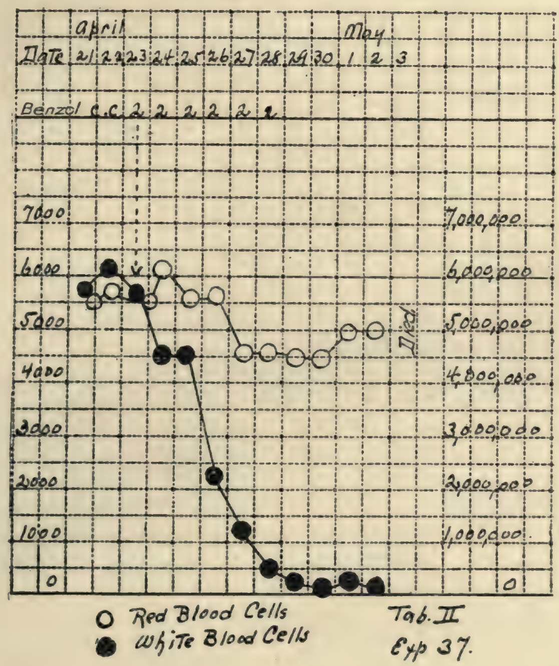


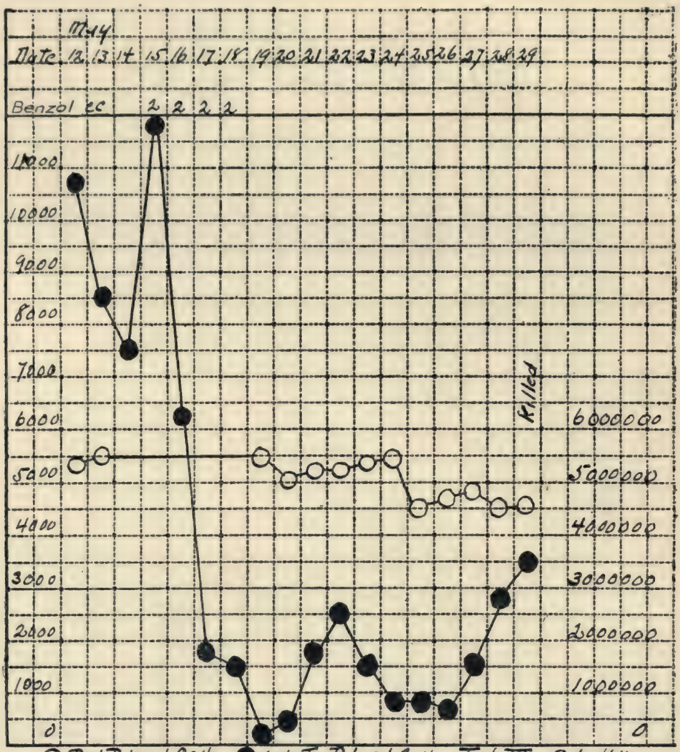
Chart IV represents the average leucocyte count of all cases from day to day during the injections.

In Chart V, using the average figures, is given the percentage loss of cells from day to day.

Here it will be seen that 24 hours after the second injection over 50% of the white blood cells have disappeared from the circulating blood, and 24 hours after the third injection almost 75% of these cells have disappeared. After the fourth injection, the relative decrease becomes less marked.

B. WHITE BLOOD CELLS. SERIES II (FATAL CASES).

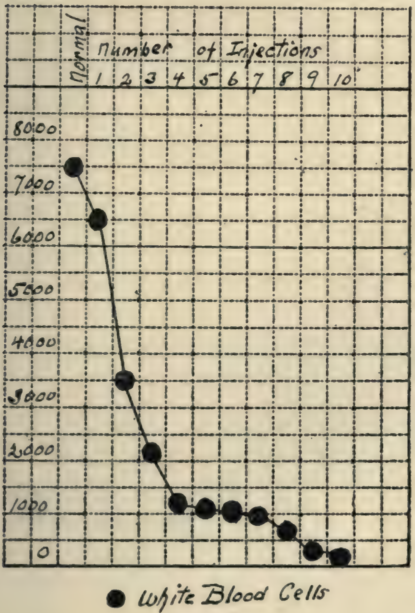
In the fatal cases after stopping the injections at a point where the white blood cells varied between 40 and 720 per cmm., the count either continued to drop or remained practically constant until death, which occurred between one and six days.



○ Red Blood Cells ● White Blood Cells. Tab III Exp. 44.

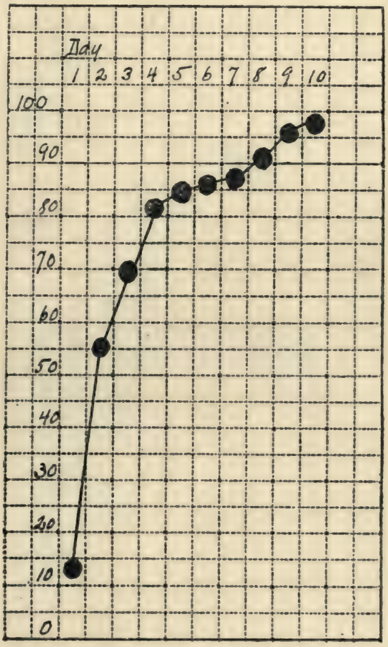
B. WHITE BLOOD CELLS. SERIES III (ASCENDING).

In the ascending series there was considerable variation in the individual experiment. The most general type was that in which after the cessation of the injections, there was a preliminary rise, followed by a fall, and then again by a second rise which continued slowly but steadily towards the normal count. Chart III illustrates this course of events. In other cases, however, the count remained very constantly low for several days, and in still others rose rapidly from the start. These variations are undoubtedly dependent upon two factors; first, the rapidity of the regenerative changes in the hæmatopoietic organs and second, the amount of poison still present in the circulating blood. Owing to the slowness of absorption of the poison, the second factor was probably subject to considerable variation.



Tab. IV.

Average loss of leucocytes from day to day during the injections.



Tab. V

Percentage loss of leucocytes from day to day during the injections.

DIFFERENTIAL COUNTS.

Differential counts are given for two cases, one in the descending series, Exp. 35, and one in the ascending series, Exp. 44. In general, where the white blood count was over 1000 cells per cmm., 250 cells were counted. Where below 1000 cells per cmm. 100 cells were counted. In each case is given the differential count made before the beginning of the injections (normal).

Exp. 35.—*Killed Twenty-four Hours After Eighth Injection.*

Number of injections. White blood count.	Normal	2	3	4	5	6
Polynuclear amphophile	44.	58.0	54.0	36.0	1.0	9.0
Polynuclear eosinophile	2.4	2.0	1.0	0.0	0.0	0.0
Polynuclear basophile	0.4	0.8	0.0	0.0	0.0	0.0
Small lymphocyte	43.2	32.4	35.0	61.0	86.0	74.0
Large lymphocyte	0.4	0.8	1.0	0.0	1.0	8.0
Large mononuclear, transitional	8.8	5.2	8.0	0.0	10.0	5.0
Unclassified	0.8	0.8	1.0	1.0	2.0	4.0
While cells per cmm	7000	3800	1560	1000	360	840

Exp. 44.—*The Counts are Given Following the Cessation of Injections. Four Injections Only Were Given in this Case.*

Day of recovery.	Normal	1	2	3	4	5	6	8	9	10	
White blood cells	9000	280	440	1880	2480	1520	840	720	1720	2800	3400
Polynuclear amphophile	54.0	25.0	15.0	53.2	82.0	48.0	43.5	8.0	24.0	40.0	42.0
Polynuclear eosinophile	4.6	0.0	0.0	0.4	0.4	0.0	0.5	0.0	0.0	0.8	0.0
Polynuclear basophile	3.7	0.0	0.0	0.0	0.0	0.0	1.0	1.0	1.2	0.0	1.6
Small lymphocyte	33.0	68.0	76.0	38.0	14.8	43.6	47.0	74.0	62.4	53.2	47.2
Large lymphocyte	0.7	1.0	4.0	1.6	1.2	1.2	1.5	0.0	1.6	1.2	1.6
Large monon. and transitional	3.6	5.0	2.0	4.0	0.4	3.2	5.0	15.0	10.0	4.8	8.0
Unclassified	0.4	1.0	3.0	2.8	0.4	3.6	1.0	2.0	0.8	0.0	0.0
Amphophilic myelocytes	0.0	0.0	0.0	0.0	0.8	0.4	0.5	0.0	0.0	0.0	0.0
Normoblasts	0.0	0.0	0.0	0.0	1 cell	0.0	0.0	0.0	1 cell	3 cells	0.0

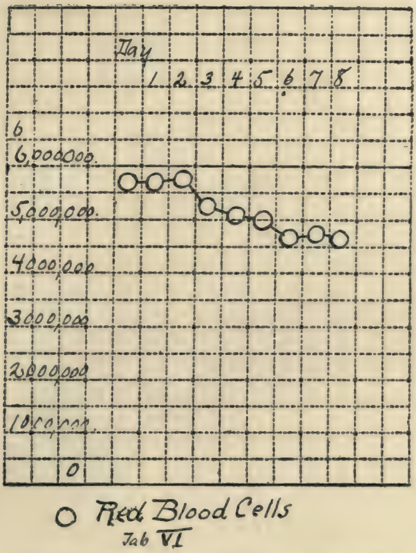
The chief point of interest is the relatively greater involvement of the polynuclear elements, than of the lymphocytes. In Exp. 35, there is at first a relative increase in polynuclears, followed by a very rapid decline in their numbers. During recovery (Exp. 44), the relations are variable, but there is a tendency for the polynuclear amphophiles and small lymphocytes to resume their normal proportions. The number of normoblasts represents the number of these cells seen in counting 250 white blood cells.

Many of the white blood cells, both of the polynuclear and mononuclear type, show advanced degenerative changes. This is evident especially in partial solution of the chromatin, with resultant marked pallor and deformity of the nucleus.

C. RED BLOOD CELLS.

In a small percentage of cases the red blood count showed a rise following the first injection. This might or might not be followed by a still greater rise after the second injection, but in all cases, the third injection brought the count back to its original level, or below that level. Langlois and Desbouis (see page 8) obtained a transient polyglobulia following the administration of benzol by inhalation. With subcutaneous injections their results were inconstant.

The behavior of the red blood cells is shown in the various charts. In the majority of cases following the second or third injection the count began to fall, but there was great variation in the individual cases. At times the fall failed to appear until after the fourth or fifth injection, and in two cases the count remained practically constant throughout. Chart VI gives the average red blood cell counts from day to day during the injections.



Average counts of the red blood cells from day to day during the injections.

From this it will be seen that the diminution in the number of red blood cells is by no means comparable to that of the leucocytes. At the end of eight days the former have lost 16% of their original number, the latter 92%.

During the period of recovery (Series III) the red blood count remained fairly constant. In some cases there was a slight further fall, in many, no change. It is noteworthy also that while the white cells were returning to normal, the red cells showed no similar tendency. (See Charts III and IV.)

D. SUMMARY.

Following the administration of benzol, there is a rapid disappearance of the white cells from the peripheral circulation preceded in some cases by an initial rise in the count. In the most advanced cases practically no white blood cells persist.

This phenomenon might be explained by (1) accumulation of the leucocytes in other parts of the circulation, or (2) death of the cells. The first possibility is excluded by the absence of white blood cells in the blood vessels throughout the body. Therefore these cells have been destroyed, and the question arises whether the destruction is due to a killing off of the cells by the poison, or to cell death from natural causes, with failure of regeneration. As will be seen, the hæmatopoietic organs suffer so greatly, as to be incapable of effective cellular reproduction as long as the poison is being administered.

As to the natural life of the white blood cells little is known. Nakanishi,[30] using a method of vital staining, found that in blood removed from the body and kept on ice for two weeks, a considerable percentage of the leucocytes remained viable. On warming, these cells showed amœboid movements. Nakaniske's observations would render it very improbable that 75% of the leucocytes would die in three days, even in the absence of regenerative changes; and this, together with the presence of many degenerated forms among the white cells, as demonstrated in smears made from the ear vein,* suggest the probability of those cells in the circulating blood by the poison. Helber and Linser[20] have shown this to be true in animals exposed to the action of Roentgen rays.

Differential counts show a greater reduction in the number of polymorphonuclear elements than in the mononuclear elements. This corresponds to the fact that the bone marrow is more severely injured than the lymphadenoid organs. After exposure to Roentgen rays (see Introduction p. 9) the lymphocytes suffer more than the polymorphonuclear cells, and here the lymphadenoid organs are more involved than the bone marrow. In neither condition are any abnormal elements found in the circulating blood.

The red blood cells are much less intensely affected than the white blood cells. In some of the cases, the count remains practically constant from the beginning to the end of the experiment, and the average of all cases shows a loss of only 12% during the first week. Such a fall is no more than could be accounted for by natural cell death,* in the absence of regeneration.

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* It is probable that some of these degenerated forms represent cells swept out from the injured bone marrow.

In a few cases, however, there is a very decided fall; and in these it is probable that the presence of the benzol in the circulation has been a factor. The increase in the pigment content of the spleen is not great, and in part at least, is referable to the great destruction of nucleated red cells in the marrow. Heineke obtained similar results following exposure to Roentgen rays. In both series of experiments there were only slight changes in the red blood cells in spite of advanced aplasia of the marrow. This would suggest the correctness of the view that the natural life of the erythrocytes is relatively long.

After the cessation of the injections, the red blood cells generally remain fairly constant. They show much less tendency than the white blood cells to return to normal. In contrast to this the erythroblasts are often very much more abundant than the granulocytes in the bone marrow, during the early stages of regeneration.

IV. Bone Marrow.

A. DEGENERATIVE CHANGES.

Exp 29.—Killed 24 hours after the first injection.

The low power appearance of the marrow is fairly normal, that is, a large central zone about the central sinus is occupied almost wholly by fat cells, while the parenchyma elements are confined to the more peripheral portions of the sections. In these peripheral regions, the cellular elements have undergone a very definite increase in numbers. Under the high powers it is seen that the increase in the parenchyma cells—the hyperplasia—affects all the elements more or less uniformly. Large lymphocytes and megaloblasts are not numerous.

Everywhere the parenchyma elements show abundant mitotic figures, evidencing an active proliferation. As yet only a small percentage of the cells show signs of injury.

The type of hyperplasia is that most common in adults—the more highly differentiated types are chiefly concerned in the proliferation, while large lymphocytes and megaloblasts are less affected.

* Grawitz[16] states, that, according to the general conception, the life of a red blood cell is from 3-4 weeks. This would allow for a loss of 25-33% of the red cells in a week.

Exp. 28.—Killed 24 hours after second injection.

The hyperplasia has advanced further than in the preceding case, so that now the entire marrow, from periphery to central sinus, is cellular (Fig. IV). The cells lie in thick, dense anastomosing masses, separated by groups of fat cells, by dilated and engorged capillaries and by œdematous reticulum. The type of hyperplasia is similar to that described in the last section.

Many of the parenchyma cells show signs of karyolysis and karyorrhexis. In some the nuclei are pale, and the chromatin partially dissolved; in others the chromatin lies in broken clumps and masses. Similar chromatin masses are found lying free in the tissue, or collected in the bodies of phagocytic cells. A considerable percentage of the myelocytes, both amphophile and eosinophile, and of the large lymphocytes, show these degenerative changes. Amphophilic myelocytes are the predominating cells.

Polymorphonuclear leucocytes, both amphophile and eosinophile, are present in relatively much smaller numbers than in the preceding experiment. In a few of them, degenerative appearances similar to those described for the myelocytes, are seen, but the great majority look normal.

The nucleated red cells share in the changes due to the poison. In many the nuclei are deformed, shrunken, pyknotic and irregular, and in others there has been a partial solution of the chromatin.

Megacaryocytes are increased about in proportion to the general hyperplasia, but many of them show advanced grades of caryolysis and caryorrhexis. They show well-marked phagocytic activity, including within their cytoplasm one or more polynuclear leucocytes in various stages of digestion. Often the injested cell is surrounded by a round, clear non-staining zone.

Mitoses are not as abundant as in the preceding experiment.

In addition to the cells described, there are found scattered everywhere, but perhaps most numerous about the periphery, cells with a dark, round, rather deeply staining nucleus, about the size of the nucleus of a small lymphocyte, and relatively abundant deep staining protoplasm. The protoplasm often shows a lighter staining zone about the nucleus, and presents short stumpy processes. These cells undoubtedly belong to the group of polyblasts (Maximow[29]). Pigment-containing cells are also present in small numbers.

	W. B. C.	R. B. C.
Normal	12,000	5,000,000
Before death	3,720	5,200,000

Although the polynuclear cells show relatively few signs of degeneration, they are nevertheless much less abundant than before, so that it seems probable that many of them have been swept out into the circulating blood.

Exp. 26.—Killed 24 hours after fifth injection.

As an evidence of hyperplastic changes, parenchymal elements are present not only peripherally, but throughout the section. As evidence of the destruction, the cells, instead of lying in dense groups and masses, are found only in small broken bands and strings, in groups of twos and threes, or wholly isolated. Between the groups lie relatively large amounts of œdematous reticulum and many fat cells. The total cell content of the marrow is sub-normal (Fig. II).

All the cell types share the degenerative changes. Amphophilic myelocytes still predominate. The polynuclear amphophiles, although fewer in numbers, show a smaller percentage of degenerative forms. Eosinophiles, both myelocytic and polynuclear, have become very scarce. Nucleated red cells are not numerous. For the most part they are found singly, or in small scattered irregular groups, and many of those remaining, are degenerated. Megacaryocytes are greatly reduced in numbers, and few normal looking exemplars are still to be found. Mitotic figures are relatively scarce, and not a few of them are abnormal.

Besides these cell types are cells resembling the small lymphocytes of the blood, and others similar to the polyblasts described in the last section. The former will hereafter be referred to simply as small lymphocytes. There seems to be no tendency for these cells to occur in groups—they lie isolated, separated from each other, and often totally independent of any parenchymal elements. Phagocytes containing nuclear detritus and pigment granules are present in small numbers.

	W. B. C.	R. B. C.
Normal	5,250	5,700,000
Before death	1,040	4,470,000

Exp 33.—Killed 24 hours after seventh injection.

The section shows much more marked changes than any of those preceding Destructive processes have far outstripped the proliferative, so that very few specific bone marrow cells persist. Parenchymal cells, isolated or in groups of two or three are found scattered at relatively wide intervals in the œdematous reticulum. All parenchymal elements are scarce but of those present the polynuclear amphophiles are most abundant. A large percentage of them now shows signs of degeneration. Amphophile myelocytes are few, and nucleated red cells are found only in small, widely scattered groups. A few megacaryocytes persist in more or less degenerated form. Large lymphocytes and eosinophile cells are practically absent.

As in the preceding sections, small lymphocytes and polyblasts are present. Phagocytes containing brown-yellow pigment and nuclear fragments are present in fair abundance.

	W. B. C.	R. B. C.	
Normal	6,000	6,200,000	..see Chart P.
Before death	720	5,450,000	

Exp. 39.—Nine injections. Died a few hours after last injection.

This experiment may stand as the representative of a considerable group of animals which either died, or were killed at about the same stage.

The marrow shows almost absolute aplasia (Fig. III). In the cross section of the femur marrow, only 1-2 parenchymal cells are to be found, and these are always degenerated. The blood vessels are dilated and contain normal looking erythrocytes, an occasional lymphocyte and no polynuclears. The reticulum is œdematous, fat cells few and shrunken. The nuclei of the connective tissue cells and endothelial cells are well preserved although some of them are swollen and pale. Besides these, one finds cells whose occurrence has been constantly noted in the previous sections of partial aplasia.

(1) Many small lymphocytes. These lie in the adventitial coats of the blood vessels, in the connective tissue capsule of the marrow and scattered through the reticulum. Usually they are isolated and rarely occur in groups. They show no sign of degeneration.

(2) Polyblasts. The majority of these approach the plasma cell type. They have a small eccentrically placed nucleus, rich in chromatin, and about the size of the nucleus of the small lymphocyte. In some two small nuclei are seen. The protoplasm is dense, distinctly basophilic, and in it close to the nucleus a lighter staining zone is often to be made out. Such cells may be pear shape, round or oval, or provided with short, stumpy processes.

(3) Pigment containing cells. These are relatively large cells, with light staining vesicular nucleus, and abundant protoplasm. They may be round, oval or spindle shaped, or provided with irregular processes. Many brownish-yellow, coarse pigment granules are present in the cytoplasm and sometimes along with these, are other granules which take a faint to deep blue stain. A few yellow pigment masses are also present extracellularly.

Summary.—This section shows the final stage of the poisoning—an almost complete aplasia of the marrow. Even the more resistant polynuclear amphophiles have disappeared. Aside from the fixed tissue cells the only elements represented are small lymphocytes, and polyblasts. These two cell types have been found in all the experiments of the descending series, but because of the uncertainty regarding their source and significance it seems preferable to discuss them separately from the parenchymal elements.

In general the polyblasts approach the plasma cell type. The small lymphocytes are in no way distinguishable from those of the circulating blood. They are found occasionally in the form of a close packed group in the adventitial coat of the large arteries, or collected about a small vessel. Both cell types, however, are much more common as isolated examples, lying in the connective tissue capsule of the marrow or scattered through the reticulum. They are separated from each other and independent of the parenchymal elements.

The question arises as to the source of these cells. Pappenheim,[42] Dominici [13] and others state that small lymphocytes are a constituent of the normal marrow, but in adult life they are present in very small numbers. Occasional plasma cells may be found in the marrow in normal conditions.

(1) Are the cells seen in the section under consideration normal constituents of the marrow, rendered visible by the destruction of the parenchymal elements? The chief fact against the assumption of this view, is the relative abundance of cells of both of these types.

(2) Are they the normal constituents which have proliferated? A study of the regenerative stages will show that regenerating cells in the bone marrow tend to assume an island or group-like arrangement. Even the polynuclear leucocytes, which have very great amœboid powers, show this grouping in many cases. But the lymphocytes here, while occurring very occasionally in the form of groups about a blood vessel, are much more common as isolated examples, scattered through the reticulum.

(3) Are they derived from the clasmatocytes? A study of Section 39, where the parenchyma elements have practically disappeared, shows that cells which may be classed as clasmatocytes are present in relatively small numbers. Those present show no signs of mitotic activity, and no especial relation to the lymphocytes and polyblasts.

(4) Are they derived from the lymphocytes of the circulating blood, as described by Maximow for the similar cells in chronic inflammatory conditions? As will be seen, the lymphadenoid tissue throughout the body is injured by the poison, and many of its constituent cells, both large and small lymphocytes are killed. It is, however, less severely affected than the myeloid tissue. In the latter stages of the poisoning, though all the cells of the circulating blood are reduced in numbers, among those persisting, the lymphocytes greatly predominate and even in these stages, occasional lymphocytes may be found wandering through the wall of one of the bone-marrow capillaries.

Of the possibilities suggested a study of the material at hand points to the last as the most probable, but the question cannot be definitely answered. *The point of chief interest, however, is that in benzol poisoning the small lymphocytes and polyblasts, during the degenerative process, whatever their source may be, are the most resistant of all the parenchymal cells. They persist and apparently increase in numbers, after all other bone-marrow elements have disappeared.**

B. REGENERATIVE CHANGES.

In discussing the regenerative changes in the marrow it is impossible to take the experiments in the order either of the number of injections or of the number of days following the cessation of injections, as the variation in the individual case is too great. We can simply describe the various stages, beginning with the earliest, giving at the same time the facts as to the experiment.

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* In this connection it is of interest to note that in Heinecke's experiments (see Introduction) both large and *small lymphocytes* were the first cells to disappear from the marrow.

Exp. 38.—Ten injections. Died 72 hours after last injection.

The low power appearance of the marrow is much like that of the preceding section. The effect of the poison is shown in œdema, hyperæmia and aplasia. In some portions, this aplasia is practically complete, in others, especially the peripheral regions, parenchymal cells are found. The cells at the periphery do not occur singly, or in indefinite rows of two or three separated from each other by wide intervals. *They form distinct groups and islands, definitely circumscribed, and appearing under the low power as small blue zones, sharply demarcated from the surrounding areas of pink staining, œdematous reticulum.* They suggest at once the picture of hæmatopoiesis occurring in the mesenchymal tissues of the embryo, as described, for example, by Saxer,[45] Maximow[31] and others (see Introduction).

In this experiment the effect of the poison is still being felt, and many cells in the islands show degenerative changes. Therefore the details of the regenerative process will be described in the following sections.

	W. B. C.	R. B. C.
Normal	8,000	5,800,000
Injections stopped	160	3,640,000
Day of death	180	2,088,000

Exp. 53.—Seven injections. Killed 4 days after last injection.

Exp. 50.—Five injections. Killed 6 days after last injection.

The sections give evidence of very severe toxæmia. There has been great cellular destruction, and even now, 4-6 days after the cessation of injections, large areas remain in which the aplasia is almost complete. Such areas contain only reticular and endothelial cells, small lymphocytes and polyblasts. The capillaries are dilated and engorged with blood, the fibers of the reticulum spread apart by œdema, and the fat cells are shrunken and deformed.

Scattered about without ascertainable relation to any definite zone are small cell nests and groups, more or less sharply circumscribed, and usually wholly isolated from one another. Here and there, where two such groups lie closer together, there is some intermingling of their cells about the margin of contact (Figs. V and VI).

Among these cell nests two types may be distinguished under the low power: one containing cells with small dark nuclei and composed of nucleated reds, the other containing larger paler cells and composed of granulocytes.

The cell nests thus described are extravascular, and many lie in immediate contact with the wall of one of the capillaries or thin-walled veins. The innermost cells lie against the endothelium and from here the cells may either spread along the vessel wall or be heaped up in a direction at right angles to it.

Erythroblastic Nests (Fig. XIX).—These are small, sharply circumscribed islands, composed of a compact group of 3-5 to 12-15 cells. In them are to be found all the types of erythroblasts: the younger forms with their relatively large pale nuclei and scanty basophilic protoplasma; the typical normoblasts, with the smaller, deeper staining nucleus and more abundant protoplasm; and the older cells with pyknotic nuclei of round, clover or rosette forms. The normoblasts are the predominant elements; but the younger forms are fairly abundant, and may either accompany the normoblasts or form independent islands.

Granulocytic Islands (Fig. XVIII).—In contrast to the erythroblastic islands are others whose outlines are more irregular and whose cells are less compact, larger and paler staining. These are the granulocytic groups, composed of large lymphocytes (myeloblasts), myelocytes, metamyelocytes and polynuclears. Myelocytes and metamyelocytes predominate, but in most of the groups myeloblasts and polynuclear elements are associated with them in varying proportions. Among the granular cells, amphophiles are much more abundant than eosinophiles, the latter being very scarce. In some of these groups the cells have a fairly close arrangement, but in most they tend to lie a little separated and small bands and streamers of cells pass out from the periphery of the group. Where such nests lie close together the outlying processes unite, and form an irregular network.

Large Lymphocytic Nests.—In addition to the granulocytic and erythroblastic nests are found a few which are composed entirely of large lymphocytes. In general they contain few cells 3-8, and in their structure are almost as compact as the erythroblastic foci. The component elements vary considerably in size, have a relatively large pale nucleus, with a distinct nucleolus and a small amount of very basophilic non-granular protoplasm.

Lying scattered irregularly between these islands are to be found isolated cells, representing the various cell types. Amphophilic myelocytes are most abundant, but large lymphocytes (Fig. XVIII, d) are fairly numerous and occasionally a large erythroblast is found. In all the cell islands, and in the isolated cells, mitotic figures are abundant. As in the descending series, small lymphocytes and polyblasts are everywhere present as isolated examples.

Megacaryocytes.—The giant cells, too, show evidence of regeneration, though they are not present in great numbers. They occur singly or in groups of 2-3 cells, closely approximated to each other. Often several such smaller groups lie together, making up a large island of perhaps 10/12 cells. Among these may be seen not only the adult type, with its much convoluted nucleus and abundant protoplasm, but also younger cells in which the nucleus is still round and the protoplasm relatively scanty. Between these and the fully developed cell, all transitional stages may be found, as they have been described, for example, by Saxer.[45]

Phagocytic cells, containing bright yellow to dark yellow pigment are present in fair abundance throughout the section. Similar pigment is to be found in many endothelial cells. In the blood vessel, white blood cells are not numerous. The lymphocytes are relatively much more abundant than the polynuclears.

	Exp. 50.		Exp. 53.	
	W. B. C.	R. B. C.	W. B. C.	R. B. C.
Normal	8,500	5,000,000	7,000	4,650,000
Injections stopped	800	4,280,000	880	4,600,000
Day of death	1,080	4,380,000	530	4,536,000

The sections show an aplastic marrow in which lie small circumscribed cell groups and islands of three types, composed of erythroblasts, granulocytes or large lymphocytes. While myelocytes (amphophiles) predominate in the granulocytic islands, and normoblasts in the erythroblastic islands, the younger cell types are present in fair numbers.

A comparison of this picture with those subsequently described, leaves no doubt that this represents early regenerative changes in a marrow that has suffered advanced aplasia.

Exp. 51.—Eight injections. Killed 5 days after last injection.

There is hyperæmia, marked œdema and almost total absence of fat cells. The cell content of this marrow is considerably below the normal, but much greater than that in Sections 50 and 53 just described. The cells are collected about the peripheral half of the section, leaving the central portion almost free. The whole of the periphery is not, however, uniformly involved. Segments densely infiltrated with proliferating parenchyma cells alternate with others relatively poor in such cells, while here and there a segment occurs, in which almost complete aplasia persists.

In the cellular zones, the island formation is typically seen. Most of the islands are erythroblastic. They are much larger than those previously described, groups of 20-30 cells being common, and where these large nests are abundant, they fuse with each other, making an irregular wide meshed network. The cells composing the erythroblastic islands may be any type from the large young forms with relatively vesicular nucleus and scanty basophilic protoplasm through the normoblasts, to the old, pyknotic cell with abundant hæmoglobin-containing protoplasm. Although normoblasts predominate, the younger elements are still very abundant. Occasionally an isolated erythroblast is found lying in the reticulum between the islands. Granulocytic regions are much scarcer. Only in one part of the section is a large group of these cells to be made out. It shows a loose branching arrangement, its streamers invading the regions between the erythroblastic nests. The component cells are chiefly amphophile myelocytes and metamyelocytes with a considerable proportion of large lymphocytes still present. Polynuclear cells of all types and eosinophilic myelocytes are very few. Aside from this large focus smaller white blood cell groups are found scattered here and there, and between them lie isolated cells of the various types.

Megacaryocytes are relatively very abundant. They occur in 4 or 5 large groups each composed of from 5-10-12 cells, and also here and there as isolated examples. As before the stages of development may be traced, and occasional mitotic figures are found. Small lymphocytes are found scattered throughout, whereas polyblasts are less abundant than in previous sections. Mitotic figures are everywhere very abundant.

	W. B. C.	R. B. C.
Normal	9,500	4,700,000
Injections stopped	640	3,745,000
Day of death	1,120	3,168,000

Summary.—In spite of the fact that the number of injections of benzol was greater than in experiments 50 and 53 and the time allowed for recovery was about the same the regenerative processes have advanced much further here.

Zones of complete aplasia still persist, but they are fewer and smaller than before. Parenchymal elements are much more numerous. They still show the island formation but the islands have increased in size and there is more tendency to fusion of adjacent groups. Myelocytes (amphophilic) and normoblasts are the predominant elements in the granulocytic and erythroblastic islands respectively, but the younger cells are still fairly abundant. The erythroblastic islands are much more numerous than the granulocytic, while islands composed of large lymphocytes are not found. Megacaryocytes are abundant.

Between the islands lie isolated cells of the different types, chiefly granulocytic, but with an erythroblast here and there. Among these one also finds small lymphocytes and polyblasts. Mitotic figures are remarkably abundant, evidencing the activity of the regenerative changes.

Exp. 46.—Killed eight days after fifth injection.

In this section the proliferation has advanced still further. Lying in the œdematous reticulum are 10-12 large blue staining, more or less circular islands, composed of parenchymal cells (Fig. VII). Though each has attained considerable size, so as to contain several hundred cells, the individual foci are separated by wide areas, in which the aplasia is well marked. There is no uniformity about their arrangement—they may be central, intermediate or peripheral. All show a structure which seems characteristic of the large regenerating foci: they form not a solid compact mass, but a fairly dense network. This results from a tendency of the cells to grow along the capillary wall, rather than through the intercapillary reticulum, and in thus following the lines of the capillary bed, they form coarse groups of anastomosing cell cords, rather than solid cell masses. This mode of growth is well seen about the margin of each focus where bands of cell cords push out from the main cell mass in more or less spoke-like arrangement (Fig. VII). With one exception all the larger foci described are pure cultures of granulocytic cells. Scattered about close to the periphery of these foci may be found usually one or more typical, small erythroblastic islands, and in only one of the large foci do groups of the two cell types occur together. Here it seems as if the proliferating granulocytic focus had grown through a region previously occupied by rather small erythroblastic islands.

In addition to these large granulocytic islands another type of growth is seen, in which these cells lie in anastomosing cords radiating in from periphery to center (Fig. VIII). Where this development is well advanced, the cords extend all the way from the capsule to the central sinus; where less advanced they are confined chiefly to the periphery. The cause of this elongated network is again the tendency of the cells to grow along the line of the capillaries. In these cell groups the relation to the blood vessel is especially well seen, almost every cord lying in definite contact with the endothelium of a thin-walled vessel. The individual strands may be either erythroblastic or granulocytic, the former predominating.

Lying scattered in small numbers between the large granulocytic foci are typical small islands such as have been seen in the previous section. They may be granulocytic or erythroblastic.

As to the composition of the large granulocytic foci, they contain all the cells of the granulocytic series, from the myeloblast to the fully developed polynuclear leucocyte. Here are great groups of amphophilic myelocytes, there great groups of amphophilic polynuclears and in other parts the two types are intimately intermingled. Myeloblasts are relatively much less numerous than in the previous sections; they do not form independent islands, but are found scattered among the more highly differentiated cells. Eosinophilic myelocytes and polynuclears are relatively scarce. All types, too, are to be found in the peripheral network as well as in the small islands. Among these erythroblastic cells, normoblasts greatly predominate. Many show small, pyknotic nuclei. In not a few these nuclei have undergone partial solution, leaving a pale structure, with a deep blue crescent or ring about its margin. Bodies staining exactly as do these partially dissolved nuclei are found, lying free in the tissue, often in large groups, or contained in the bodies of phagocytes.

Megacaryocytes: giant cells are exceedingly abundant in this preparation. They occur in small numbers enclosed within the large, regenerating, granulocytic groups, but far more abundantly about the margins of such groups or between two adjacent groups. There seems no regularity or arrangement about their distribution. Here they occur singly—there in large nests of 10-15 cells. Such a nest contains cells of varying types, from those whose nuclei are dark, and almost naked, to those whose nuclei are pale, and whose protoplasm is abundant. Phagocytosis of round cells and polynuclears occurs frequently, and there is evidence of amœboid activity. in the presence of long irregular processes going out from some of the cells. Nuclear figures, both uni- and multipolar are to be found, and many of the megacaryocytes show evidence of more or less advanced degeneration, in crumbling of the protoplasm and partial solution of the nucleus.

Pigment is present in fair amounts, and many phagocytes contain both pigment and the nuclear rests before described. Small lymphocytes and polyblasts may be found scattered here and there. Throughout the section mitosis is very active.

	W. B. C.	R. B. C.
Normal	3,000	4,800,000
Injections stopped	720	3,900,000
Day of death	720	4,000,000

Summary.—The regenerative changes have advanced much further in this experiment. Small aplastic zones are still present, but the parenchymal elements are much more abundant than before. They may occur as:

(1) Large circular islands containing several hundred cells.

(2) Anastomosing networks of cords radiating in from periphery to central sinus.

(3) Small scattered islands.

(4) Isolated cells.

The large islands are almost pure cultures of granulocytic cells. They form a coarse network rather than a solid cell nest, owing to the tendency of the cells to grow along the line of the capillary bed rather than through the intercapillary reticulum. The more highly differentiated cell types, myelocytes, metamyelocytes and polynuclears greatly predominate.

The anastomosing network of cords about the periphery contains granulocytes and erythroblasts in about equal numbers, again with the older cell types in greater abundance. As before the formation of the network is due to the tendency of the proliferating cells to follow the line of the capillary bed. Apparently the growth here proceeds from periphery to center; for where the development has not advanced far, the cell cords lie chiefly in the peripheral zone, often with one end immediately against the capsule of the marrow.

The small scattered islands and the isolated cells between them, are similar in all respects to those described in previous sections. Mitosis is very active. Megacaryocytes are very abundant, and are found in all stages of development. Many show phagocytic activity, and some have pseudopod-like processes evidencing amœboid activity. Unipolar and multipolar mitosis are found in some of the cells.

The chief features of interest are the great size of the granulocytic islands, the marked tendency of both types of cells to grow along the walls of the capillaries, and the increasing predominance of the older cell types.

Exp. 47.—Killed 7 days after eighth injection.

In some of the segments the marrow is beginning to have a hyperplastic appearance, thick anastomosing cell cords filling up the reticulum from periphery to center. In other segments the arrangement resembles rather that described in Exp. 46. Here and there are small zones which are still wholly or almost wholly aplastic. They are found constantly in relation to an artery of medium size, which may lie centrally or eccentrically in the aplastic area. About every one of the larger arteries in the section, such a zone of relative or absolute aplasia is found. Granulocytes and erythroblasts are equally abundant. Among these the younger cell types are relatively scanty.

	W. B. C.	R. B. C.
Normal	6,500	5,700,000
Injections stopped	720	5,223,000
Day of death	720	3,504,000

Exp. 44. Killed 11 days after the fourth injection (Chart III).

The section shows great hyperplasia, parenchymal cells filling practically the whole of the marrow. Fat cells are scattered here and there in small numbers. In one area, about two rather small arteries, is an area of relatively well-marked aplasia, and here the reticulum still shows evidence of toxic œdema. All cell types have proliferated, and are present in abundance.

	W. B. C.	R. B. C.
Normal	10,000	5,000,000
Injections stopped	280	5,130,000
Day of death	3,400	4,144,000

Exp. 41.—Killed 15 days after ninth injection.

The entire picture is one of extreme hyperplasia, parenchymal cells being closely packed together in a dense mass throughout the entire section. Fat cells are not abundant. The chief components of the hyperplastic marrow are represented by polynuclear leucocytes and normoblasts.

	W. B. C.	R B. C.
Normal	6,000	5,600,000
Injections stopped	520	5,616,000
Day of death	5,920	5,672,000

Exp. 56.—Killed 3 days after fifth injection.

Parenchymal elements are present in considerable abundance. For the most part there is no sharp marking off of cell groups and islands; no sharp contrast between islands of two types, lying close together but distinctly separated. Instead, the cells occur in diffuse groups connected with each other by cords and strands or scattered irregularly throughout.

Foci of nucleated red blood cells are found in relatively small numbers, but where present they resemble erythroblastic foci found in other experiments. They consist chiefly of normoblasts with well preserved nuclei, and a relatively small percentage of the younger cell types. The erythroblasts are over-shadowed by the great numbers of granulocytes present. Among them typical polynuclear leucocytes greatly predominate. Next in frequency are metamyelocytes while myelocytes are less abundant and large lymphocytes relatively very few. All these cells may occur in ill-defined groups, or scattered in twos and threes throughout all parts of the section. Eosinophiles are scarce. Megacaryocytes are present in small numbers, as well as many small lymphocytes and polyblasts.

	W. B. C.	R. B. C.
Normal	10,000	4,800,000
Injections stopped	840	....
Day of death	3,000	4,010,000

Summary.—This experiment must be compared with 50 and 53 which represent in general a corresponding duration of recovery. It differs from these in

(1) The abundance of parenchymal elements.
(2) The great predominance of the more highly differentiated cells.
(3) The absence of island formation.

The rapid development of the large number of cells of the older types (polynuclears, metamyelocytes and normoblasts) corresponds to what is found in the normal adult marrow, when such a marrow is stimulated to increased activity. And so the phenomenon would seem to have its explanation in the persistence of a large number of parenchymal elements capable of further growth and mitotic activity. That is, the aplasia in this case never reached an advanced grade, as it did, for example, in Sections 50-53. Accompanying the rapid increase in parenchymal elements, the white cells of the circulating blood have increased from 840 per cmm. to 3000 per cmm. in the three days following the cessation of injections.

GENERAL SUMMARY.

Benzol (C_6H_6) causes a destruction of the specific bone-marrow cells. A series of injections results in an extreme aplasia of the marrow.

As in the case of many other poisons, it acts not only as a destructive agent, but also as a stimulant, and throughout the descending series, stimulation and destruction are constantly associated. At first the former prevails, and the parenchymal elements increase rapidly in numbers (Fig. IV). As in hyperplasias of normal adult marrows, the increase is chiefly in the more highly differentiated cell types. The younger forms, myeloblasts and megaloblasts are less affected.

In this hyperplastic marrow, cell destruction is well marked by the end of the second day. From this time on, as successive doses are given, an increasing number of cells is injured. The injured elements gradually disappear, leaving the cell cords broken and irregular. They lie separated from each other by wide areas of œdematous reticulum and dilated capillaries. Eventually only isolated cells or small groups of two or three remain. Following the ninth injection the marrow is almost wholly aplastic (Fig. III). All the cell types, erythroblasts, granulocytes and megacaryocytes are injured by the poison. With the exception of the polymorphonuclear elements, all seem to be affected to about the same extent. In the polynuclear amphophiles, the proportion of degenerating cells is always less than in the other cell types. Nevertheless they decrease very rapidly in the marrow after the second injection. This is probably due to the fact that they are swept out into the circulating blood in large numbers. For this reason the amphophilic myelocytes, although more susceptible than the polynuclears, are the prevailing cells during the earlier stages.

In all these specimens of the descending series small lymphocytes and polyblasts are found scattered through the reticulum in considerable numbers (see summary, Exp. 39). The source of these cells, whether normal constituents of the marrow or cells that have wandered in from the blood vessels, could not be determined. But whatever their source they show greater resistance to the poison than do the parenchymal elements—they persist, and apparently increase in numbers after all the other cells have been destroyed.

After the cessation of the injections, regenerative processes begin, and result in the return of the marrow to normal. The rapidity with which regenerative changes become manifest, varies in the different cases. Where the poisoning has been less severe (Exp. 56), the injured cells are rapidly replaced by proliferating groups of normal cells. Where the poisoning has resulted in a marked aplasia, 3-6 days are required for the onset of effective regeneration. The difference is dependent upon two factors, (1) the number of parenchymal elements persisting, and (2) the quantity of benzol in the circulation at the time the injections cease.

In the early stages of regeneration the cells appear in the aplastic reticulum in the form of circumscribed islands and groups (Figs. V, VI, XVIII, XIX). These are more or less widely separated, are extravascular and often lie in contact with the wall of the capillary. They may be composed of erythroblasts, granulocytes or large lymphocytes, the erythroblastic islands being the most numerous. Between these islands lie isolated cells of the various types, as well as small lymphocytes and polyblasts. With the progress of regeneration, the islands increase in size and number (Fig. VII). They lie close together, and adjacent groups tend to fuse. The type of cell, erythroblastic or granulocytic, remains constant after proliferation has begun. In addition to the larger and smaller islands, there is another type of growth in which cell cords, starting at the periphery, grow inward toward the central sinus in radiating bands.

During the entire regenerative process, megacaryocytes are present. They may occur isolated through the tissue or form distinct islands. In these islands are found not only fully developed cells with complex nuclear picture and abundant protoplasm, but also the younger forms in which the nucleus is round or oval, and the protoplasm relatively scanty. From this type to the fully grown cell, all transitions may be traced. Multipolar and unipolar mitosis are found. Some of the cells are phagocytic and some show evidences of amœboid activity.

In the early stages, although the more highly differentiated cells (myelocytes, polynuclears and normoblasts) predominate, the younger forms (large lymphocytes, myeloblasts, megaloblasts) are relatively abundant. As regeneration advances the younger cells persist, but form an ever diminishing proportion of the cell content of the marrow. Throughout all stages, isolated cells of all the different types are constantly found lying between the islands.

The subsequent events consist simply of a continuation of the process above described, so that in from 10-18 days after the cessation of the injections, the marrow has not only regained its original cell content, but has become hyperplastic and packed with cells from periphery to center.

A comparison of the descending series with the earlier specimens of the ascending series makes it evident that regeneration can occur in a marrow which has reached an advanced grade of aplasia.

As has been said, the early regenerative changes are characterized by the formation of small circumscribed cell nests and islands. The formation of such islands in an aplastic marrow can have but one explanation—that each island develops from a single parent cell. What is the source and nature of this parent cell?

Owing to variations in the effect of a given number of doses of the poison, it cannot be assumed in any case that all of the marrow cells have disappeared before the onset of regeneration. A few parenchymal cells, still capable of mitotic activity, probably persist in each case. The persistence of these cells might serve to explain the erythroblastic and granulocytic islands, or at least, some of these islands. But in the earlier stage of regeneration, large lymphocytes are also present in considerable abundance both in the form of islands and scattered through the tissue. In the normal adult marrow relatively few of these cells are found, and during the administration of the poison, they degenerate along with the other cell types. So it must be assumed that at the time of cessation of the injections, they are very scarce. What then is the origin of these cells? In view of the destructive changes that have preceded, the large lymphocytes of the early regenerative stages seem much too abundant to justify the view that they are derived from persisting large lymphocytes.

As to other sources of origin the fixed tissue cells (connective tissue and endothelium) can be excluded. At no time do they show signs of activity; at no time are mitotic figures found among them, and no transitional forms are seen. What is true of the fixed tissue cells is equally true of the clasmatocytes, as was pointed out in Section 39 (summary). This leaves the small lymphocytes and polyblasts. As has been stated, these cells occur in considerable number in all of these specimens of the descending series. Their source could not be definitely ascertained. But whether they are persisting parenchymal elements or derivatives of the small lymphocytes of the circulating blood, they are the most resistant of all the cell types, and are present after all other cells have disappeared. Their distribution, as scattered, isolated examples corresponds to the distribution of the cells in the regenerating marrow, and it seems very possible, even very probable, that they play the chief rôle in the regenerative changes. A conversion of small lymphocytes into large lymphocytes would explain fully the abundance of the latter cells and the occurrence of such a change is generally admitted as a physiological process, as, *e. g.*, in the lymph glands. Further differentiation of the large lymphocytes thus formed into cells of the erythroblastic and granulocytic series, offers no difficulties for those who hold the monophyletic theory. Maximow[30] has demonstrated the process in the formation of bone marrow in the kidney in rabbits.

A study of the megacaryocytes tends towards the same view. These cells arise not by division of pre-existing cells of the same type (Saxer[45]), but by further development of large lymphocytes. They are readily destroyed, but appear in the regenerating marrow in considerable numbers. Their presence again points to the abundance of the large lymphocytes in the regenerating marrow, and requires for its explanation something more than the persistence of the few large lymphocytes that might have survived. Our idea as to the most probable explanation has been given above—a conversion of the small lymphocytes to large lymphocytes and further differentiation of the large lymphocytes.

V. LYMPH GLANDS.

General.—The lymph glands, studied in each case, comprise specimens taken from the root of the mesentery, from the greater or lesser curvature of the stomach, from the inguinal region, from the superficial fascia of the thigh, and occasionally from other regions. As the changes from day to day proceed rather slowly, only such specimens will be described as seem necessary to give a general picture of the process in its more typical stages. In many cases, lymph glands taken from different regions of the same animal, show considerable differences. But, in general, these differences will not be taken into account in the descriptions, only one typical gland being described for each experiment.

A. DEGENERATIVE CHANGES.

Exp. 29.—Killed one day after first injection.

The gland looks somewhat hyperplastic, the cells being very abundant and closely packed together. The individual follicles are large, and consist chiefly of a large round or oval *Keimcentrum*, surrounded by relatively few strands of small lymphocytes. Nuclear figures are no more abundant than in the normal gland. Throughout the gland are large and small lymphocytes whose nuclei show varying grades of pyknosis, caryolysis and caryorrhexis. As a result of this degenerative process, chromatin fragments are found lying scattered through the tissue. They may be free, or contained in phagocytes (Fig. XX).

Exp. 30.—Killed 24 hours after third injection.

The *Keimcentra* in all the follicles stand out prominently as large central, paler staining, zones surrounded by relatively fewer strands of small lymphocytes. Throughout the follicular region are degenerating lymphocytes, and nuclear fragments; but they are much less numerous than in the previous section. Most of the fragments lie free, relatively few having been picked up by phagocytes. The lymphatic tissue of the follicular region is beginning to show a reduction in amount. The lymphocytes within the follicles are less compactly arranged than normal, and the entire follicular zone is a little shrunken. The medullary cords show little change.

Exp. 33.—Killed 24 hours after seventh injection.

Gland from the root of the mesentery. Nuclear fragments are somewhat more numerous than in the specimen just described. They occur both in the follicles and in the medullary cords.

The lymphocytic content of the gland is definitely reduced. The lymphocytes are very loosely arranged in the follicles, and the reticular cells and reticular network stand out prominently. The entire follicular zone is markedly flattened and shrunken. It is retracted away from the capsule, so that the peripheral sinus gaps open (Fig. XIV). At the junction of follicles and cords, the medullary sinuses are dilated and partially divide the follicular zone. Within the follicle themselves, similar dilated lymph spaces are present.

All the follicles are not injured to the same extent. Here and there one is seen which contrasts with its neighbors by a greater richness in lymphocytes. The medullary cords are less affected.

Exp. 35.—Killed 24 hours after the eighth injection.

The follicles are not all involved to the same extent. Some few preserve a fairly normal appearance; others show a considerable decrease in the content of lymphocytes—a decrease which may be more marked either in the periphery, or in the center (Figs. XIII, XIV). In those that have been most severely injured, the lymphocytes have almost wholly disappeared, and the position of the follicle is recognizable only by the arrangement of the reticular network. The medullary cords show similar changes.

Exp. 39.—Died shortly after ninth injection.

The capsule is thickened and œdematous, its fibers being spread apart and infiltrated with serum. The connective tissue cells are of the fibroblastic type. About the peripheral portion of the capsule they are relatively few, but immediately about the gland substance they form a close packed cellular layer, with little intercellular substance. Between the fibroblasts lie red blood cells scattered and in groups, polynuclear leucocytes and polyblasts. Radiating in from the capsule are bands of similar tissue, separating the follicles from each other and invading the follicles themselves.

The individual follicle presents a very abnormal appearance. It is partially or completely surrounded by a capsule of young connective tissue, which encroaches on its periphery and sends sprouts into its substance. The cells within the follicle are loosely arranged and consist of small groups of small lymphocytes, a few large lymphocytes and a variable number of polyblasts and plasma cells. The medullary cords show similar changes. They are œdematous and swollen, and encroach upon the medullary sinuses. They consist chiefly of young looking cellular connective tissue, in which only occasional fibrillar bands are present. Here, too, polyblasts and plasma cells are fairly numerous lying in the tissue meshes.

B. REGENERATIVE CHANGES.

Exp. 56.—Killed 3 days after fifth injection.

The entire follicular zone is diminished in size and the lymphocytes lie widely separated in the reticular network. Here and there denser, more compact groups of lymphocytes are found, occupying a rather central position in the follicle. The surrounding regions are poor in cells, and the reticular network stands out prominently. It is possible that such compact groups of cells represent the beginning regenerative changes.

Exp. 51.—Killed 5 days after the eighth injection.

Gland from root of mesentery. The capsule of the gland is œdematous, and the connective tissue increased. Some of the lymph follicles show a reduction in size with widening of the peripheral sinuses, but in others the quantity of lymphatic tissue is not much below normal. The *Keimcentra* are not prominent, and mitotic figures not numerous.

Gland from superficial fascia of thigh. The changes in this gland taken from the same animal are much more advanced than in that just described. Both the aplasia and fibrosis are more marked. The capsule and trabeculæ, follicles and medullary cords are all involved in the fibrosis, and in places the connective tissue has grown into the medullary lymph spaces, partly or wholly obliterating them.

Exp. 47.—Killed 7 days after the eighth injection.

Gland from root of mesentery. The capsule is swollen and œdematous and contains new formed granulation tissue. The lymphatic tissue is fairly abundant, but the follicles have not fully returned to the normal size. Aside from a slight increase in connective tissue cells, they have, however, an approximately normal appearance. *Keimcentra* are rather prominent, but the mitoses in them do not seem to be much increased. There is considerable new formed young connective tissue in the medullary cords, but it is found most abundantly between the cords, where it forms a fairly close meshed network, filling up many of the medullary sinuses.

Exp. 41.—Killed 15 days after ninth injection.

Gland from root of mestentery. *The greater part of the section shows normal gland tissue* (Fig. XII). Some of the follicles, however, are small, irregularly and indefinitely outlined, retracted away from the capsule and trabeculæ, leaving very wide sinuses. Here, too, the cells are less compact. In these places the restoration to normal is not complete.

Pigment.—Fine and coarse granular pigment of yellow to yellowish-brown color is found in many of the lymph glands. The quantity and distribution varies greatly in the different experiments, and in the different glands of the same experiment. It may lie in the protoplasm of large cells which occur in groups in the follicles and medullary cords; in free phagocytes of the peripheral or medullary lymph spaces; in the bodies and processes of the reticular cells, which form a loose anastomosing network through the sinuses; and finally in the endothelial cells. Erythrocytes, sometimes free, sometimes in the bodies of phagocytes, are found in varying numbers in the lymph spaces throughout the glands. Inasmuch as normal glands show similar differences in the quantity and distribution of pigment and erythrocytes little significance can be attached to these variations and the detailed descriptions are omitted.

C. SUMMARY.

Injection of benzol causes a destruction of lymphocytes both in the follicles and medullary cords of lymph glands. Within twenty-four hours of the first injection the cells show caryolysis and caryorrhexis and chromatin fragments are found scattered through the tissues. After subsequent injections these signs of degeneration are much less marked. Part of the cell debris is picked up and digested by large phagocytic cells.

After the third injection the cell content of the follicles begins to show evident reduction. As the cells are destroyed, the reticulum in which they rested, contracts—there is a flattening out of the entire follicular zone, and an approximation of the capsular and medullary surfaces. The peripheral and medullary sinuses undergo a compensatory dilatation. With the continuation of the process, the lymphocytes become progressively less numerous and eventually only the reticulum is left to indicate the former position of the follicles. The medullary cords suffer less than the follicular zone (Figs. XIII, XIV).

By the eighth or ninth day, however, the lymph glands also show marked aplasia. But the involvement is not uniform, and even in the most advanced stages of degeneration some of the follicles retain a considerable number of lymphocytes.

After the cessation of injections there is a gradual regeneration of the lymphocytes. In the aplastic glands they appear in 3-4 days, as compact cell groups, more or less centrally located within the follicles. As they increase in numbers they fill out the reticular network, and the follicular zone regains its normal size. Within 10-15 days regeneration is complete (Fig. XII). In many of the glands, however, a complete return to normal is impossible. Owing to the irritation of the poison, granulation tissue is formed in the capsule, cords, follicles, and medullary sinuses, resulting in a well-marked fibrosis.

On the whole, the changes in the lymph glands are less marked than those in the bone marrow. Even in the most advanced stages of degeneration, some of the follicles retain a considerable number of lymphocytes and although some of the follicles do not regenerate completely until 10 or 15 days after the injections have been discontinued, others recover much more rapidly.

A comparison of the two series indicates that follicles can recover completely after they have been rendered almost entirely aplastic.

VI. Appendix (Lymph Follicles).

A. NORMAL.

Before going on to the changes occurring in the appendix it may be well to discuss briefly the normal appearance (Fig. IX), Czermack,[8] describing the appendix of the normal rabbit, says: "Excepting for the peritoneum all parts of the intestinal villi are distorted by the follicles. The muscular coat is slightly developed, the muscularis mucosæ almost wholly lacking, and the epithelium deformed in many places."

The submucosa forms the greater part of the wall of the appendix. The regions marked *a, b, c, d* in the figure (Fig. IX) represent portions of the lymphadenoid tissue of the submucosa separated for convenience in description.

(a) These are oval or polygonal structures, definitely outlined by a thin layer of connective tissue. The follicles consist of rather loosely arranged lymphocytes, both small and large, lying in a delicate reticulum.* In addition to the lymphocytes are seen the round or oval vesicular nuclei of reticular cells, occasional polynuclear amphophiles and pigment cells. The pigment cells are found in the form of round or irregular zones (Fig. IXe) of pale to deep yellow color, sharply demarcated from the surrounding lymphatic tissue. In general they lie in the periphery of the follicles. The individual cells are 10-14μ in diameter and are polygonal in shape. Their nuclei are rather small, round or oval and vesicular. The distinctive yellow color of the cell is due to the accumulation in its cytoplasm of closely packed masses of pale yellow to copper-colored granules. In any given cell neither the color nor the size of the granules are uniform. Cells of a somewhat similar appearance are frequently found in the follicles and medullary cords of the lymph glands, and in the spleen.

In addition to the cellular contents described, small numbers of nuclear fragments, varying in size and staining intensity (*tingible Körper*), are always present.

(b) Resembles the follicles of an ordinary lymph node being composed almost wholly of small lymphocytes closely packed together to form a dense mass.

(c) Here again the arrangement of the cells is looser—more closely resembling (a). The small lymphocytes are less compact and the large ones more abundant.

(d) This contains simply a compact mass of small lymphocytes.

Mucosa.—Under normal conditions many lymphocytes are found scattered through the connective tissue of the mucosa and lying between the epithelial cells which cover the villi and line the glands of Lieberkühn.

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* According to Czermack[8] the large lymphocytes which are identical with the *Keimcentrum* cells, are collected chiefly in this region, so that this really represents the *Keimcentrum* of the follicle.

B. DEGENERATIVE CHANGES.

Exp. 29.—Killed 24 hours after the first injection.

The low power appearance of the section is normal. Under the high power changes are to be seen which closely resemble those described in the lymph glands of the corresponding stage of the poisoning. They consist in a degeneration of the lymphocytes—pyknosis, caryolysis and caryorrhexis —and in the presence of chromatin masses resulting from this degeneration. A few phagocytes are found containing nuclear fragments. The lymphatic tissue is not uniformly involved; it is only region (a) that suffers to any considerable extent.

As has been seen in the appendix under normal conditions one finds many lymphocytes lying in the connective tissue of the mucosa, or wandering out between the epithelial cells of the villi and Lieberkühn's glands. In the section under consideration, the number of such lymphocytes is considerably reduced.

Exp. 30.—Killed 24 hours after the third injection.

A distinct reduction is evident in the number of lymphocytes infiltrating the connective tissue of the mucosa, and wandering out between the epithelium of the villi and Lieberkühn's glands. The follicles show a reduced lymphatic content; not only are the lymphocytes less compactly arranged than normal, but the total thickness of the submucosa is also diminished. As the lymphocytes disappear there is a general contraction of the reticulum in which they rested, so that the submucosa becomes thinned and atrophic. Such a change is analogous to what was found in the follicles of the lymph gland.

As might have been anticipated from the findings in the previous experiment, the greatest loss of cells occurs in the part of the follicle designated as (a). The lymphocytes in this region have to a great extent disappeared. Partly replacing them are found many large mononuclear cells, with round or oval, pale staining nuclei (see Fig. X) and fairly abundant pink staining granular looking protoplasm.

Cells with yellow granular pigment, such as were described in the normal appendix, are present in very small numbers.

Exp. 31.—Killed 24 hours after the fourth injection.

The section shows a striking variation from the normal—an exaggeration of the changes which were seen in the previous specimen. The connective tissue of the mucosa is very poor in lymphocytes, and only an occasional cell of this type is found migrating through the epithelium.

The submucosa shows a distinct diminution in thickness (Fig. X). The follicles which form its chief mass have everywhere lost a large percentage of their lymphocytic content. The change is least marked in (d), and by far most marked in (a) where lymphocytes are found only as isolated examples. In this part of the follicle the reticulum is filled out with large mononuclear cells like those described in a similar location in the preceding section (Fig. Xa). Here and there are cells of similar structure and appearance which contain in their cytoplasm a variable number of yellow pigment granules, and which resemble the pigment cells of the normal appendix. Between the pigmented and non-pigmented cells all transitions occur. Degenerative changes in the nuclei are frequently seen.

Exp. 38.—Died shortly after the ninth injection.

The specimen represents an extreme grade of the process which has been seen in the two previous sections (Fig. XI). In the mucosa lymphocytes occur only as exceptional examples. The submucosa bears scarcely any resemblance to the normal. It is thin and atrophic, and its lymphocytes have been almost wholly destroyed or swept out. It is only in the region designated as (d) that small groups still occur. The mononuclear cells and pigment cells, which were present before only in the basal portion of the follicle, have now invaded the entire follicle.

C. REGENERATIVE CHANGES.

Exp. 59.—Killed 2 days after the fourth injection.

The mucosa shows a few cells scattered about in the connective tissue, and wandering through the epithelium. The submucosa is perhaps one-third its normal thickness, and along with this atrophy goes a great reduction in the number of lymphocytes. As usual this reduction is most marked at the base of the follicular region. Mononuclear cells, as before described, are present here in considerable numbers, and many of them are degenerated and vacuolated. Considering that this animal had received but 4 doses of benzol, the condition of the appendix would indicate that very little regeneration had as yet occurred.

Exp. 56.—Killed 3 days after the fifth injection.

The lymphocytes are everywhere showing a tendency to increase in numbers, the cells lying closely together and the lymphatic tissue appearing somewhat more uniform. In the base of the follicle the cell content is still very low.

Exp. 51.—Killed 5 days after the eighth injection.

Regeneration is progressing rapidly. Everywhere in the follicle excepting at the base, the lymphocytes are closely packed together, and the whole appearance is uniform and regular. In these regions mitotic figures are abundant. The submucosa has returned to perhaps one-half its normal thickness. Lymphocytes in the interstitial tissue of the mucosa are not abundant.

Exp. 47.—Killed 7 days after the eighth injection.

The appearance is beginning to approach the normal. Large numbers of lymphocytes are now found in the connective tissue of the mucosa and between the epithelial cells. The lymphatic tissue of the submucosa has a uniform compact appearance, and even at the base of the follicle the lymphocytes are beginning to collect in considerable numbers. They occupy the central part of this region, while the periphery is filled with the pigmented and non-pigmented mononuclear cells. Mitosis is active.

Exp. 44.—Killed 11 days after the fourth injection.
Normal looking appendix.

D. SUMMARY.

The lymphatic tissue of the normal appendix consists of large follicles filling almost the entire submucosa (Fig. IX). The changes in this tissue, as the result of the poisoning, closely resemble those described for the lymph glands. *They consist in destructive processes leading to an advanced aplasia, and followed by a complete regeneration.* The basal portion of the submucosa (a) shows the greatest changes throughout the experiments.

After the first injection many degenerating lymphocytes are found in the submucosa. With a continuance of the injections, the lymphocytes gradually decrease in numbers, the reticulum becomes prominent, and the entire submucosa contracts. As the lymphocytes disappear the reticulum becomes partly filled with pigmented and non-pigmented large mononuclear cells (Fig. Xa). Between pigmented and non-pigmented cells all transitions are to be found, and the pigmented cells are identical with those of the normal appendix. Therefore, the filling of the reticulum by these cells does not represent invasion by a foreign element, but an increase in elements normally present. Associated with these changes there is a gradual diminution in the number of lymphocytes lying in the mucosa. *After 9 injections most of the lymphatic tissue has been destroyed and only a few scattered groups of lymphocytes persist. The submucosa has contracted to a small fraction of its original thickness* (Fig. XI).

Regenerative changes become evident 3-4 days after the cessation of injections. They consist of a reversal of the destructive process—gradual accumulation of lymphocytes in the submucosa and a reappearance of similar cells in the connective tissue and epithelium of the mucosa. As the lymphocytes increase within the follicles, they assume a more compact arrangement, and a more uniform appearance; the follicles themselves enlarge, the submucosa begins to expand and the wall of the appendix approaches its normal thickness. Within 10-14 days after the administration of benzol has ceased, the regenerative process is complete.

VII. Spleen.

A. DESCENDING SERIES.

Exp. 29.—Killed 24 hours after the first injection.

Under the low power the appearance is normal, except for a rather unusual prominence of the *Keimcentra* of the Malpighian corpuscles. Under the higher power one sees within the corpuscles, considerable numbers of lymphocytes whose nuclei are shrunken and pyknotic, and groups of chromatin fragments derived from breaking up of these cells. In the pulp, too, a few pyknotic nuclei are seen.

In the splenic sinuses are many lymphocytes and polynuclear amphophiles of normal appearance, and a few large mononuclear cells containing a finely granular yellow pigment.

The pulp cords are wide, normal looking and contain:

(1) Many typical small lymphocytes.

(2) Large cells, whose protoplasm is abundant, pale staining and of indefinite outline. The nuclei may be round, oval or horse-shoe shaped—they are large, vesicular, and very poor in chromatin. Some of these cells are phagocytic and have ingested yellowish pigment granules or occasional white blood cells. These cells will be referred to as large mononuclear pulp cells.

(3) Many red blood cells.

(4) Polynuclear amphophiles.

(5) Polynuclear eosinophiles in small numbers.

(6) Reticular cells.

The number of degenerating forms is much less than in the corresponding stage of poisoning in the lymph glands and appendix.

Exp. 30.—Killed 24 hours after the third injection.

There is a very evident loss of lymphatic tissue. The Malpighian corpuscles are much reduced in size, the lymphocytes being collected in considerable numbers only about the central vessel. The margin of this group of cells is irregular and serrated, and within the group are small spaces which are cell free. Of the cells that remain some are pyknotic, others more normal looking. The more peripheral portions of the Malpighian corpuscles is made up of reticulum, with its concentrically arranged, elongated, vesicular nuclei, among which are scattered a few small lymphocytes. Nuclear fragments are present in small numbers.

Pulp Cords.—All the elements of importance, lymphocytes, large mononuuclear pulp cells, polynuclear amphophiles and red blood cells, are still present. But their numbers are diminished leaving the cords thinner than normal, and the reticular and endothelial nuclei relatively more prominent. Some of the polynuclears show pyknosis and caryorrhexis. Degenerating lymphocytes are also present, but in smaller numbers.

Sinuses.—The sinuses are not dilated. Their content in both lymphocytes and polynuclears is reduced, and in both cell types some are found which show degeneration.

Summary.—The section shows a definite loss of lymphatic tissue. In the Malpighian corpuscles lymphocytes are present in considerable numbers only about the central vessel. All the cellular elements of the pulp cords are reduced. Fewer lymphocytes and polynuclear amphophiles are present in the sinuses than before.

Exp. 27.—Killed 24 hours after the sixth injection.

The specimen shows more marked changes than any of those previously examined. In the Malpighian corpuscles the lymphocytes are greatly reduced in number, only a few fairly compact rows surrounding and accompanying the central artery. Elsewhere the reticular framework of the corpuscle stands out with great prominence devoid of lymphocytes. Pyknotic and degenerating cells are few. Within the meshes of the reticulum are seen a few polyblasts and plasma cells (Fig. XVI).

The splenic pulp shows analogous changes. The pulp cords are thin and delicate and are composed chiefly of the collapsed reticulum in which lie red blood cells. The lymphocytes, the large mononuclear pulp cells and the polynuclear amphophiles are found only here and there as isolated examples (Fig. XVII).

The endothelial nuclei bulge well into the sinuses, which are packed with erythrocytes. Here again the lymphocytes are scarce, but even so, they are much more abundant than polynuclear amphophiles. Degenerated examples of both are present. Mitotic figures are rare.

Exp. 39.—Died a few hours after the ninth injection.

In this specimen are found the extreme changes resulting from repeated doses of the poison. Under the low power, the Malpighian corpuscles are lighter in color instead of darker staining than the surrounding tissue. They show the central vessel lying in the loose meshed reticular framework with its elongated, oval vesicular nuclei. In the meshes of this network are a few scattered lymphocytes.

Pulp Cords.—In place of wide cords, composed of loose reticulum and packed with red blood cells, lymphocytes, etc., one finds a thin, collapsed, compact wall. In this wall the meshes of the reticulum are narrow so that the endothelial and reticular nuclei seem more numerous than normal Between them lie a few isolated erythrocytes. Here and there in the connective tissue at the junction of a group of sinuses, the red blood cells are more numerous, and a few lymphocytes or an occasional large mononuclear pulp cell may be found (Fig. XVII).

Sinuses.—The sinuses are dilated, filled with blood, and contain extremely few lymphocytes. Neither here nor in the pulp cords are there any polynuclear leucocytes.

The section shows almost total aplasia of the spleen. Lymphocytes are present in extremely small numbers in the Malpighian corpuscles, the pulp cords and the sinuses. Polynuclear amphophiles are wholly absent.

B. REGENERATIVE CHANGES.

Exp. 53.—Killed 4 days after the seventh injection.

The Malpighian corpuscles show a considerable number of lymphocytes collected in fairly uniform, compact masses, immediately about the central vessel; whereas, the peripheral portion of the follicle contains relatively few such cells, and the total lymphocytic content of the follicle is much below normal. The *Keimcentra* are not prominent and mitoses are not numerous.

The pulp cords are thinner than normal and the reticular and endothelial nuclei stand out prominently because of the diminution in the other cellular elements. Of the other elements erythrocytes are present in considerable numbers, but lymphocytes are only to be found here and there in small groups. Polynuclear amphophiles are scarce, while large mononuclear pulp cells are only occasionally found.

The sinuses are not dilated. In addition to red blood cells they contain everywhere small numbers of lymphocytes and a few polynuclear amphophiles.

Considering the number of injections—7—a comparison with the corresponding specimen in the descending series will show that regeneration is already well under way. Though the lymphocytes are still reduced in number, they are much more abundant than the polynuclear elements, both in the sinuses and pulp cords.

Exp. 52.—Killed 5 days after the fifth injection.

The Malpighian corpuscles are rapidly returning to normal. The amount of lymphatic tissue, while still considerably reduced, is much greater than in the preceding specimen.* Here and there in the corpuscles are found small groups of polyblasts and plasma cells. Mitotic figures are not abundant.

The pulp cords are wider and the reticular cells less conspicuous. Among them lie many erythrocytes and a fair number of lymphocytes, polynuclears and large mononuclear pulp cells. In the sinuses, too, lymphocytes and polynuclears show a decided increase over the preceding specimen.

Exp. 44.—Killed 11 days after the fourth injection.

Regeneration has advanced further than in the preceding specimens. The Malpighian corpuscles have an almost normal appearance. The pulp cords are wide and their cell content is little reduced (Fig. XV). In the sinuses white blood cells are increasing in numbers, the lymphocytes still being more abundant than the polynuclears.

Scattered in small numbers throughout the section, singly and in groups of 3 and 4, are cells which have not been observed in any of the spleens before described. The predominant element in these groups is a large round or somewhat oval cell, 12-15μ in diameter. The nucleus is relatively large, and may be round, oval or slightly horse-shoe shaped, with a delicate chromatin reticulum. The characteristic feature is the protoplasm which contains a uniformly distributed, closely packed mass of fine lilac granules (H and E). The entire appearance closely resembles that of the amphophilic myelocyte of the bone marrow (Fig. XXIII). Along with these, or occurring separately are small groups of cells of similar structure, but whose bodies are filled with coarse, bright red granules—eosinophilic myeolocytes (Fig. XXIIIg). The cells here described may be found either free in the sinuses or in the reticulum of the pulp cord. They are absent from the Malpighian bodies, although here and there an isolated myelocyte is found lying among the outermost rows of lymphocytes, which bound the corpuscle. Everywhere in the spleen the sinuses contain many nucleated red blood cells, and along with them, a few typical bone-marrow megacaryocytes.

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* In comparing this specimen with that preceding the difference in the number of injections must be taken into account; and the more normal appearance of this spleen is probably due as much to the smaller number of injections as to the extra day allowed for recovery.

The nucleated red blood cells are chiefly such as have relatively small, pyknotic nuclei and abundant protoplasm—that is, the older rather than the younger type of erythroblasts. They lie within the sinuses, more or less evenly distributed throughout the entire organ. In many places they present a remarkable picture—they no longer appear as rounded disks, but show instead, an hour-glass or dumb-bell form (Figs. XXI, XXIIc). One end of the dumb-bell lies within the pulp cord; it is composed entirely of chromatin, and varies in size from a mere chromatin fleck, to a mass almost as large as an entire normoblastic nucleus. From this a delicate chromatin strand passes through the sinus wall * and into the sinus. Here it enters the body of the normoblast, and terminates in a bulb-like swelling, which consists of the remainder of the nucleus of the normoblast. The amount of nuclear material in the cell body varies in inverse proportion to the amount in the pulp. The length of the chromatin strand varies; usually it is short, but in some cases it may reach 6-7μ.

The cell body may retain its normal shape or be drawn into the form of a triangle (Fig. XXIc). In the latter case, the chromatin strand passes out from the apex of the triangle. In none of these cells does the protoplasm accompany the chromatin strand through the sinus wall. All the protoplasm lies within the sinus, and both the strand and the chromatin mass in the pulp cord are extracellular. All of the nuclei which show these changes

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* According to Weidenreich[54] the wall of the sinus is completely closed and consists of: (a) on the inner side, long slender endothelial cells running parallel to the long axis of the sinus. They are not directly connected with each other, but are separated by relatively wide spaces. (b) A very thin structureless membrane upon which these cells rest. This membrane shows stomata due to the passage of colorless corpuscles. (c) Thick cylindrical fibers belonging to the reticulum of the pulp cords, and running in planes at right angles to the endothelial cells.

take a uniform deep blue stain and show no structure. An occasional cell resembling these dumb-bell normoblasts is found in the sinuses. Here one also finds a few naked nuclei (Fig. XXIf). As has been mentioned, nucleated red blood cells of the ordinary type are found in the sinuses, but practically no such cells are found in the pulp cords. In the cords, however, lie a considerable number of naked normoblastic nuclei.

Summary.—Regeneration is almost complete. In addition to its normal cells, the spleen contains amphophilic and eosinophilic myelocytes, megacaryocytes and nucleated red cells. Among the nucleated red cells are many which show a dumb-bell form, the protoplasm with part of the nucleus, forming one end of the bell, and lying within the sinus. The remainder of the nucleus (naked) composes the other end of the bell and lies within the pulp cord. These two ends are connected by a strand of chromatin which forms the constriction passing through the sinus walls.

Exp. 41.—Killed 15 days after the 9th injection. The regenerative changes in the spleen are practically complete (Fig. XV).

Scattered here and there in the pulp are seen a few cells which resemble in all respects those described in the previous section as amphophilic myelocytes. The presence of these cells, together with small numbers of normoblasts and megacaryocytes, suggests a beginning myeloid metaplasia. Eosinophilic myelocytes are absent.

A small number of normoblasts shows the dumb-bell form, and the same relation to pulp, sinus, and sinus wall, as was shown by very many of the erythroblasts in the section previously described.

Exp. 42.—Killed 19 days after the fifth injection.

The general structure and appearance of the spleen corresponds to the normal. The process of regeneration is complete. There is, however, a myeloid metaplasia, somewhat less marked than in Section 44.

Pigment.—In all the sections of the spleen, yellow to yellow-brown pigment is present in varying amounts. It occurs chiefly in the pulp cords, either free or in the bodies of phagocytes. To a less extent pigment cells are found in the sinuses and peripheral zones of the Malpighian corpuscles. The later specimens show a somewhat greater pigment content than the earlier ones, but at no time is there very much increase over the normal.

SPLEEN. GENERAL SUMMARY.

The changes in the spleen produced by the poison are similar in type to those found in the lymph glands and appendix. They consist essentially of a gradual loss of parenchymal elements ending in an almost complete aplasia of the organ, and followed by complete regeneration. In addition, there are two points of interest: (a) myeloid metaplasia occurring in the later regenerative stages, and along with this (b) *a peculiar relation of the nucleated red blood cells to the sinus wall.*

Following the first two injections, the *Keimcentra* appear unusually prominent. Nuclear fragments and degenerating nuclei, are much less numerous than in the corresponding stages of the poisoning in the lymph glands. This difference is hard to explain in view of the fact that the ultimate result of the poisoning is similar in the two organs. The degenerating cells are found chiefly within the Malpighian corpuscles and to a lesser extent within the pulp cord. Few of these degenerated cells are picked up by phagocytes.

In the Malpighian corpuscles, the lymphocytes disappear first from the periphery of the follicle, leaving a compact group of cells around the central vessel. As the poisoning continues the cells about the central artery gradually diminish in number (Fig. XVI), and after 9 injections the lymphocytes are practically all destroyed, the position of the follicle being recognizable only by the arrangement of the reticulum and the central vessel.

Associated with the changes in the Malpighian corpuscles, there is a destruction of parenchymal cells in the pulp cords. Lymphocytes, large mononuclear pulp cells and polynuclears gradually disappear. The reticulum contracts and the cords become shrunken and collapsed, rendering the reticular and endothelial cells more prominent (Fig. XVII). In the later stages, even the erythrocytes are swept out. The aplasia of the cords becomes practically complete by the end of the ninth day, *i. e.,* coincident with the aplasia of the Malpighian corpuscles. This is of importance because the changes in the cords do not become evident as early as those in the follicles. The difference is probably due, not to a difference in the effect of the poison on the two parts of the spleen, but to the fact that slight changes are more readily recognized in the follicles than in the cords.*

After the cessation of injections, there is a gradual increase in the parenchymal elements of the pulp cords and the Malpighian corpuscles. Within 10-15 days the spleen presents a practically normal picture. A comparison of experiments 41 and 39 indicates the regenerative power possessed by the spleen. In Exp. 39 is seen an almost absolute aplasia a few hours after the ninth injection; in Exp. 41 a normal spleen is found 15 days after the ninth injection (Fig. XV).

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* Heinecke observed in his experiments, also, that the Malpighian corpuscles were affected sooner than the pulp cords. It is probable that, as in our cases, the difference is dependent on the greater difficulty of detecting early changes in the pulp cords.

In the last animals of the ascending series, those killed respectively 11, 15 and 19 days after the final administration of the poison, there has been a myeloid metaplasia of the spleen—that is, the development of typical bone-marrow elements, represented by amphophilic and eosinophilic myelocytes, normoblasts and megacaryocytes (Fig. XXIII g, h). The myelocytes occur isolated and in small groups intermingled with the normal elements of the pulp and sinuses. The nucleated red blood cells and the megacaryocytes are found within the sinuses.

Such a myeloid metaplasia has been frequently described in the recent literature (see Introduction). According to Meyer and Heinecke [34] and Domarus,[11] myeloid tissue in the spleen is of autochthonous origin; it represents a return of the organ to its embryonic function of hæmatopoiesis and is compensatory in nature. Sternberg [40] is inclined to the view that in many cases the presence of myeloid cells is referable to the function of the spleen as a blood filter, rather than to its function as a hæmatopoietic organ. In the cases described above, an autochthonous origin of the cells seems more probable, for the number of immature blood cells (myelocytes, normoblasts) found in the circulating blood is very small.

As to the compensatory nature of the process the total number of myeloid cells found in the spleen is not great, and when one considers the extreme hyperplasia of the bone marrow in the corresponding experiments it seems improbable that the spleen could have added much to the regeneration of the blood.* As pointed out by Meyer and Heinecke [34] the red spleen pulp alone—cords and sinuses—is involved in the process. The Malpighian bodies are not affected, although in the specimens above described an occasional isolated myelocyte is found in the extreme periphery of the follicle.

Among the nucleated red blood cells are many which have a dumbbell shape, and lie partly within the sinus, partly within the pulp cord. The part lying within the pulp cord consists of a naked nucleus, and is extracellular. From it a strand of naked chromatin passes through the sinus wall into the sinus, where it enters the cell body. Here it joins the remainder of the nucleus, which is surrounded by all the cell

* Blood counts on day of death in these cases were:

	R. B. C.	W. B. C.
Exp. 40	4,144,000	3,400
Exp. 41	5,672,000	5,920
Exp. 42	4,256,000	4,000

protoplasm. Within the pulp cords lie naked nuclei, but practically no nucleated red blood cells (Figs. XXI, XXII, XXIII).

Three possibilities suggest themselves as an explanation of this picture. It may represent:

I. Diapedesis of the nucleated red blood cells.
II. An active migration of the cell.
III. An extrusion or wandering out of the nucleus from the cell body.

I. *Diapedesis.*—There is a striking resemblance to the pictures seen in the capillaries of a frog after ligation of the larger veins into which these capillaries empty. In the vascular bed behind the ligature the capillaries and veins become packed with nucleated red blood cells.* Following this, diapedesis occurs (Thoma [52]) and many nucleated red blood cells may be found sticking in the walls of the capillaries and constricted into hour-glass form † (Fig. XXIV). The first portion of the cell to pass out consists chiefly or wholly of protoplasm. It may or may not contain a small portion of the nucleus. The entire nucleus, or the remaining portion, as the case may be, is left within the lumen of the capillary. It is *not,* however, a *naked* nucleus, but a *nucleus surrounded by a well-marked zone of protoplasm.* So there is a division of the cell *body* into two parts, associated with which the nucleus may or may not be divided. In other words, *no part of the nucleus is extracellular.* Nucleated red cells are found free in the tissues about the dilated capillaries.

Comparing the two phenomena, then, we find in the frog that (1) as a result of marked congestion of the capillaries, diapedesis occurs: (2) during the process the cell body is always divided into two portions, whereas the nucleus may or may not be divided; (3) no part of the nucleus is extracellular; (4) nucleated red cells are found free in the tissues. On the other hand, in the case of the rabbit's spleen above described, (1) there is no congestion to account for diapedesis; (2) the nucleus is always divided into two parts, the cell body never; (3) part of the nucleus is always extracellular; (4) practically no nucleated red cells are found in the pulp. So, in spite of the apparent similarity between the two pictures, the differences in the conditions of occurrence, and the differences in the details of the process, justify us in considering that the basic phenomena in the two cases are different.*

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* For an opportunity to examine and picture this process in the frog, the author is indebted to the kindness of Professor Marchand, to whom he wishes to express his thanks.

† The red blood cells of the frog are larger than those of the rabbit, are oval in shape and are all nucleated.

II. *Active Migration of Nucleated Red Blood Cells.*—In the spleen, lymphocytes are often found wandering through the sinus walls (Fig. XXIIIk). If, like the lymphocytes, nucleated red cells are actively migrating, the question arises in which direction the movement is taking place. Supposing them to be passing from pulp to sinus, then it is necessary to assume that practically all the protoplasm passes through first—for examples are seen in which the protoplasm lying within the sinus contains merely a pin point fleck of chromatin, connected by a chromatin thread with the bulk of the nucleus which lies naked within the pulp cord (Fig. XXIIIc). This process would predicate an almost complete forcing of the nucleus out of the cell protoplasm during the passage of the cell through the sinus wall. The completion of the migratory act could only take place by the wandering of this nucleus through the sinus wall and back into the cell body.

If the migration is in a direction from sinus to pulp, then, in view of pictures of the same type (where practically all the nucleus lies naked within the pulp cord, a mere fleck of chromatin persisting in the cell body) it would be necessary to assume that first, almost the entire nucleus wandered out of the cell body, through the sinus wall and into the pulp, and then, by means of a delicate connecting band of chromatin drew the cell body after it, and finally wandered back into the cell from which it arose.

It is obvious that both these possibilities present very serious difficulties—seem in fact to be impossibilities. In addition, as was mentioned before, almost all the nucleated red cells lie within the sinuses; practically none are found in the pulp cords, a fact which speaks strongly against a migration in either direction. And, finally, no evidence has been brought forward suggesting that the older form of nucleated red cells have amœboid properties. Löbenhoffer[28] suggests the possibility for the younger forms, but gives no proof. Thayer,[57] in a recent paper, describes amœbic movements in cells of the megaloblastic type. This author was enabled to follow the amœboid movements in freshly drawn blood, under the microscope.

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* It is of interest to note that Weidenreich[54] states that, while diapedesis of erythrocytes is generally assumed, he could find no pictures suggesting it in the spleen, though figures showing migration of colorless corpuscles were very abundant.

The cells described in these sections as having an hour-glass form, are cells with homogeneous, diffuse staining nuclei and abundant protoplasm—that is, the older and not the younger types. All these points are against the interpretation of the phenomenon as an active migration of nucleated red blood cells.

III. *Extrusion or Active Migration of the Nucleus Out of the Cell Body.**—In favor of this are those very points which oppose the view of diapedesis or of active migration of the entire cell.

(1) The fact that *all the protoplasm always remains in the sinus, irrespective of the relations of the nucleus.*

(2) That the portion of the nucleus within the pulp is always *naked nucleus,* nucleus which has already passed out of the cell body. As has been said, almost the entire nucleus may lie in the pulp cord, and a mere fleck of chromatin remain in the protoplasm. Pictures of this type give the impression that the nucleus is just about to pull wholly away from the normoblast, leaving it an erythrocyte.

(3) The extreme scarcity of nucleated red blood cells in the pulp.

(4) The presence in the pulp, in considerable numbers, of naked normoblastic nuclei (Figs. XXI, XXIIIf).

These facts render it necessary to discard the first two possibilities, and accept the third. The pictures here seen represent a migration of the nucleus out of the body of the red blood cell and thus support the extrusion theory as opposed to that of intracellular degeneration of the nucleus. It does not exclude the occurrence of intracellular degeneration in nucleated red blood cells elsewhere in the body.

It is not supposed that this migration of the nucleus out of the cell body occurs only in relation to the wall of the splenic sinuses. Here and there, within the sinuses themselves and in many places in the bone marrow, pictures are seen suggestive of a similar process. But in no other place can the relations between nucleus and cell body be so accurately and certainly determined, and nowhere else do they speak so definitely for the conversion of the erythroblast to the erythrocyte by an *active wandering out of the nucleus.*

VIII. OTHER ORGANS.

A study of the other organs of the body reveals little of importance. The liver and kidney show varying grades of fatty degeneration. In addition in some of the cases, hæmorrhages are found in the wall of the stomach and intestine and in the lungs.

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* The literature on this question has been discussed briefly in the Introduction.

GENERAL SUMMARY.

Summarizing briefly the results of the experimental study of benzol poisoning, the chief points of interest are:

(1) Benzol is a powerful leucotoxin. It destroys the white cells of the circulating blood, and the parenchymal cells of the hæmotopoietic organs.

(2) Myeloid tissue is injured more than lymphadenoid tissue, and corresponding to this, the polynuclear leucocytes of the circulating blood are more affected than the lymphocytes. The erythroblastic tissue of the bone marrow is destroyed, but the circulating erythrocytes are injured relatively little.

(3) By repeated injections of benzol, the myeloid and the lymphadenoid tissues can be rendered almost wholly aplastic.

(4) Cessation of the injections at a point where the hæmatopoietic organs are almost wholly aplastic is followed within 3-4 days by beginning regenerative changes. Within 10 days to 3 weeks these organs have completely regenerated. As regeneration takes place the blood picture approaches the normal.

(5) The regenerative process in the bone marrow begins with the formation of small, circumscribed cell groups and islands, composed of large lymphocytes, granulocytes or erythroblasts. In any given island, after cellular differentiation has once begun, the type of cell, whether erythroblast or granulocyte remains constant. The islands increase in size and number, fuse with each other, and lead to a complete filling of the reticulum with parenchymal elements. In the earliest stages the younger cell types (myeloblasts and megaloblasts) are relatively abundant. In the later stages these cells are still present, but, in comparison with more highly differentiated cells, they are relatively scarce.

(6) The polynuclear amphophiles in the marrow are more resistant than large lymphocytes, myelocytes, erythroblasts and giant cells. But more resistant than the polynuclear amphophiles are typical small lymphocytes and polyblasts. These two cell types are found after all other bone-marrow cells have disappeared. Their source, whether they are derived from the lymphocytes of the circulating blood or represent

normal marrow constituents, could not be determined definitely. But whatever the source, these small lymphocytes apparently play an important rôle in the regenerative process. It seems probable that this rôle consists in a conversion of small lymphocytes to large lymphocytes, and further differentiation of the large lymphocytes into granulocytes, erythroblasts and megacaryocytes.

(7) During the later stages of regeneration, myeloid cells of all types are found in the spleen. They are relatively few in number, and the bone marrow in the corresponding cases is hyperplastic. Therefore the myeloid metaplasia can have had little significance as a compensatory phenomenon. Considering the great scarcity of myelocytes and normoblasts in the circulating blood, it is probable that the myeloid tissue in the spleen is autochthonous in origin.

(8) In many of the normoblasts found in the spleen in these cases, pictures are seen which can be interpreted only as *active migration* of the nucleus out of the cell body. The conversion of the erythroblast to the erythrocyte by a wandering out of the nucleus must therefore be admitted as a physiological process.

In closing, I wish to express my thanks to Drs. M. C. Winternitz and G. H. Whipple for their kind assistance.

DESCRIPTION OF FIGURES.

The microphotographs (Figs. I-XVII) were made in the Pathological Institute in Leipzig. For his assistance in preparing these, I wish to thank Dr. M. C. Winternitz, of the Pathological Department of The Johns Hopkins Hospital.

Fig. I.—Normal bone marrow of rabbit. Towards the lower portion of the picture is seen the fatty tissue in the region or the central sinus. Magn. 93 diam.

Fig. II.—Well-marked aplasia of the marrow following the sixth injection of benzol. The parenchymal cells are greatly reduced in number, and occur singly and in small groups. Many of them are degenerated. Well-marked œdema of the reticulum and deformity of the fat cells.

Fig. III.—Advanced aplasia of the marrow following 9 injections. Well-marked œdema and hyperæmia. Magn. 93 diam.

Fig. IV.—Beginning hyperplasia of the marrow following the second injection. The parenchymal elements are arranged in coarse irregular groups. Large cell groups are seen about the central sinus. Magn. 93 diam.

Figs. I, II, III, IV are all taken with the same magnification, and at corresponding points—so as to include a portion of the central sinus. They can therefore be directly compared with one another.

Fig. V.—A regenerating marrow in the early stages, showing the islands of erythroblasts (a) and granulocytes (b). A myeloblast (c). Polyblasts (d). Magn. 430 diam.

Fig. VI.—Early regenerating marrow, showing islands of normoblasts in an otherwise aplastic reticulum. Magn. 175 diam.

Fig. VII.—Later stage of regeneration, showing large islands composed wholly of granulocytes. The islands are separated by areas of aplastic reticulum. Œdema of the reticulum. Magn. 93 diam.

Fig. VIII.—Later stage of regeneration, showing long strands of cells growing in toward the central sinus, along the course of the capillaries. The parenchymal cells are extravascular. On the right erythroblasts. On the left, granulocytes. Magn. 175 diam.

Fig. IX.—Normal rabbit's appendix. *a, b, c, d* represent various portions of the lymphadenoid tissue of the submucosa. *e* shows groups of mononuclear pigmented cells. Magn. 93 diam.

Fig. X.—Partial aplasia of the lymphadenoid tissue of appendix. The lymphocytes have almost wholly disappeared from region (a), and in their place are large mononuclear cells both pigmented and non-pigmented. The submucosa is reduced to about one-half its normal thickness (compare Fig. IX). Magn. 93 diam.

Fig. XI.—Extreme aplasia of lymphadenoid tissue of appendix. *x* represents all that remains of the submucosa. It contains chiefly large mononuclear pigmented and non-pigmented cells, and a few lymphocytes. Nine injections of benzol. (Cf. Fig. IX.) Magn. 93 diam.

Fig. XII.—Shows a normal appearing lymph gland. This section was taken from an animal which was allowed to recover for 15 days after 9 injections of benzol. Magn. 93 diam.

Fig. XIII.—Lymph gland showing advanced aplasia after 8 injections of benzol. In the upper portion of the section practically all the lymphocytes have disappeared from the follicle, leaving only the supporting tissue. Magn. 93 diam.

Fig. XIV.—Advanced aplasia of a lymph gland (from same case as XIII). Shows œdema of the capsule, dilatation of the lymph spaces, and marked loss of lymphocytes. Compare Fig. XII. Magn. 93 diam.

Fig. XV.—Normal appearing spleen, showing Malpighian corpuscles, pulp cords and sinuses. This specimen was taken from a case where regeneration had gone on for 19 days after 5 injections. Magn. 93 diam.

Fig. XVI.—Advanced aplasia of the spleen following 6 injections of benzol. In the Malpighian corpuscle the lymphocytes are greatly reduced in numbers, and the supporting tissue is prominent. The pulp strands are thin, collapsed and almost wholly devoid of parenchymal cells. Magn. 93 diam.

Fig. XVII.—A higher power picture of the same spleen, to show the thin, collapsed pulp cords. Magn. 175 diam.

Fig. XVIII.—Regenerating marrow, showing an isolated group of granulocytes. (a) Amphophilic myelocytes; (e) large lymphocytes (myeloblasts); (d) an isolated large lymphocyte. Leitz, Oc. 3. Obj. 1/12 oil imm.

Fig. XIX.—Regenerating marrow, showing groups of erythroblasts; (a) older; (b) younger cells.

Fig. XX.—Lymph gland after one injection of benzol; (a) small lymphocyte; (b) large lymphocyte; (c) chromatin fragments; (d) phagocytic cells containing chromatin fragments; (f) large lymphocyte undergoing caryolysis. Leitz, Oc. 1. Obj. 1/12 oil imm.

Fig. XXI.—Spleen. Exp. 44. (a) Splenic sinus; (b) pulp cord; (c) nucleated red blood cell, with nucleus drawn out into hour-glass form. The protoplasm with part of the nucleus lies in the sinus. From this a thin strand of chromatin passes through the sinus wall, and terminates in a bulbous chromatin mass lying in the pulp cord; (d) endothelial cell; (f) naked nucleus lying in the pulp cord. Leitz, Oc. 3. Obj. 1/12 oil imm.

Fig. XXII.—Spleen. Exp. 44. Letters represent same structures as above. In the hour-glass normoblasts (c), more of the chromatin of the nucleus lies in the pulp cord, and less within the cell body in the sinus; (e) pigment cell in sinus; (k) free pigment in pulp cord. Leitz, Oc. 3. Obj. 1/12 oil imm.

Fig. XXIII.—Spleen. Letters as in XXI, XXII. In the normoblast (c), almost all the nucleus is extracellular and lies within the pulp cord, a mere fleck of chromatin remaining in the cell body. (g) Eosinophilic myelocyte; (h) amphophilic myelocyte. Leitz, Oc. 3. Obj. 1/12 oil imm.

Fig. XXIV.—Showing diapedesis of nucleated red blood cells in a blood vessel of a frog's tongue as a result of stasis (experimental). The portion of the cell which is extravascular consists of protoplasm (a). The nucleus, surrounded by a well-defined zone of protoplasm, is seen within the vessel. Compare with (c) of the three previous figures. Leitz, Oc. 3. Obj. 1/12 oil imm.

Bibliography.

1. Aubertin, C., and Beaujard, E.: Action des rayons X sur le sang et les organes hæmatopoiétiques. Compt. rend. Soc. de biol., 1905, LVII, 217.
2. Bloch, E.: Beiträge zur Haematologie. Ztschr. f. klin. Med., 1901, XLIII, 420.
3. Blumenthal, R., and Morawitz, P.: Experimentelle Untersuchungen über post-hämorrhagische Anämien. Deutsches Arch. f. klin. Med., 1907, XCII, 25.
4. Bunting, C. H.: Experimental anæmias in the rabbit. J. Exp. Med., 1906, VIII, 625.
5. ——— The effects of lymphotoxins and myelotoxins on the leucocytes of the blood and on the blood-forming organs. Univ. Penn. M. Bull., 1903, XVI, 200.
6. Butterfield, E. E., Meyer, C., and Heinecke, A.: Ueber das Vorkommen der Altmannschen Granulationen in den weissen Blutzellen. Folia haematol., 1909, VII, 325.

7. Butterfield, E. E.: Ueber die ungranulierten Vorstufen der Myelocyten und ihre Bildung u. s. w. Deutsches Arch. f. klin. Med., 1908, XCII, 336.

8. Czermack, W.: Entwicklung, Zusammensetzung und Funktion der Lymphknoten der Darmwand. Arch. f. mikr. Anat., 1893, XLII, 581.

9. Dantschakoff, W.: Untersuchungen über die Entwicklung des Blutes und Bindegewebes bei den Vögeln. Anat. Hefte, 1908, XXXVII, 471.

10. ——— Untersuchungen über die Entwicklung des Blut u. s. w. Arch. f. mikr. Anat., 1909, CXXIII, 117.

11. von Domarus, A.: Ueber Blutbildung in Milz und Leber bei experimentellen Anämien. Arch. f. exp. Path. u. Pharmakol., 1908, LVIII, 319.

12. Dominici, H.: Considérations générales sur la structure des apparaits hæmatopoiétiques du lapin. Compt. rend. Soc. de biol., 1900, LII, 13.

13. ——— Sur le plan de structure du système hæmatopoiétique des mammifères. Arch. gen. de méd., 1906, I, 641.

14. Ehrlich, Lazarus, Pinkus: Nothnagel's spezielle Pathologie und Therapie. 1901, VIII. Three papers.

15. Giemsa, G.: Ueber die Färbung von Feuchtpräparaten mit meiner Azureosinmethode. Deutsche med. Wchnschr., 1909, XXXV, 1751.

16. Grawitz, E.: Klinische Pathologie des Blutes. 1906. Third edition.

17. Gruber, G. B.: Beziehung der Milz und Knochenmark zu einander. Arch. f. exp. Path. u. Pharmakol., 1907, LVIII, 289.

18. Heinecke, A.: Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlung auf innere Organe. Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1905, XIV, 21.

19. ——— Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlungen auf den Knochenmark. Deutsche Ztschr. f. Chir., 1905, LXXVII, 196.

20. Helber, C., und Linser, P.: Experimentelle Untersuchungen über die Einwirkung der Röntgenstrahlen auf das Blut. München. med. Wchnschr., 1905, XV, 680.

21. Hirschfeld, H.: Ueber Leukanämie. Folia haematol., 1906, III, 332.

22. ——— Ueber einen Fall schwerer haemorrhagischen Diathese mit Knochenmarkatrophic. Folia haematol., 1906, III, 429.

23. Howell, W. H.: The life-history of the formed elements of the blood. J. Morph., 1891, IV, 57.

24. Israel, O., und Pappenheim, A.: Ueber die Entkernung der Säugetier-erythroblasten. Virchow's Arch., 1896, CXLIII, 419.

25. von Kölliker, A.: Ueber die Blutkörperchen eines menschlichen Embryos, u. s. w. Ztschr. f. rat. Med., 1846, IV.

26. Langlois, J. P., et Desbouis, G.: L'action des vapeurs de benzol sur le sang. Hygiène générale et appliqué, 1907, II, 149.

27. ——— Des effets des vapeurs hydrocarbonées sur le sang. J. de physiol. et pathol., 1907, IX, 253.

28. Löbenhoffer: Ueber extravaskuläre Erythropoese in der Leber. Beitr. z. path. Anat. u. allg. Path., 1908, XLIII, 125.

29. Maximow, A.: Entzündliche Neubildung von Bindegewebe. Ziegler's Beitr., 1902, Supplementhefte V, 1.

30. ——— Experimentelle Untersuchungen zur postfötalen Histogenese des myeloiden Gewebes. Beitr. z. path. Anat. u. z. allg. Path., 1907, XLI, 122.

31. ——— Untersuchungen über Blut und Bindegewebe. Arch. f. mikr. Anat., 1909, LXXIII, 443.

32. ——— Untersuchungen über Blut und Bindegewebe. Arch. f. mikr. Anat., 1910, LXXVII, 1.

33. ——— Der Lymphocyte als gemeinsame Stammzelle u. s. w. Folia haematol., 1909-10, VIII, 125.

34. Meyer, E., und Heinecke, A.: Blutbildung bei schweren Anämien und Leukämien. Deutsches Arch. f. klin. Med., 1907, LXXXVIII, 435.

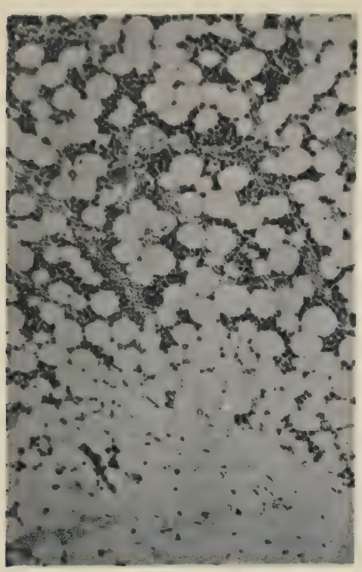
35. ——— Ueber Blutbildung in Milz und Leber bei schweren Anaemien. Verhandl. d. deutsch. patholog. Gesellsch., 1906, IX, 224.

36. Morawitz, P., und Rehn: Ueber einige Wechselbeziehungen der Gewebe in den Blutbildenden Organen. Deutsches Arch. f. klin. Med., 1908, XCII, 109.

37. Morris, R. S.: Blood formation in liver and spleen in experimental anæmias. Johns Hopkins Hosp. Bull., 1907, XVIII, 198.

38. Naegeli, H. W.: Blutkrankheiten und Blutdiagnostik. Leipzig, 1908.
39. Nakanischi, K.: Vorläufige Mitteilungen über eine neue Färbungsmethode u. s. w. München. med. Wchnschr., 1900, XLVII, 187; 680.
40. Neumann, E.: Ueber die Bedeutung des Knochenmarks für die Blutbildung u. s. w. Arch. f. Heilk., 1869, X, 441.
41. ——— Neue Beiträge zur Kenntnis der Blutbildung. Arch. f. Heilk., 1874, XV, 68.
42. Pappenheim, A.: Neuere Streitfragen aus dem Gebiet der Haematologie. Ztschr. f. klin. Med., 1902, XLVII, 216.
43. Rindfleisch, G. E.: Ueber Knochenmark und Blutbildung. Arch. f. mikr. Anat., 1880, XVII, 1-11; 21-42.
44. Santesson, C. G.: Ueber chronische Vergiftungen mit Steinkohlenheerbenzin. Arch. f. Hyg., 1897, XXI, 336.
45. Saxer, F.: Entwicklung und Bau normaler Lymphdrüsen. Anat. Hefte, 1896, VI, 1; 6.
46. Schridde, H.: Ueber Regeneration des Blutes under normalen und krankhaften Verhältnissen. Centralbl. f. allg. Path. u. path. Anat., 1908, XIX, 865.
47. ——— Beitrage zur Lehre der Zellkörnelung. Die Körnelung der Plasmazellen. Anat. Hefte, 1905, XXVIII, I. Abt., 691.
48. Selling, L.: A preliminary report of some cases of purpura hæmorrhagica due to benzol poisoning. Johns Hopkins Hosp. Bull., 1910, XXI, 33.
49. Sternberg, C.: Experimentelle Untersuchungen über die Entstehhung der myeloid Metaplasie. Beitr. z. allg. Path. u. path. Anat., 1909, XLXI, 586.
50. ——— Ueber das Vorkommen von einkernigen, neutrophil gekörnten granulierten Leukocyten in der Milz. Centralbl. f. allg. Path. u. path. Anat., 1905, XVI, 929.
51. Tallqvist, T. W., und Willebrand, C.: Zur Morphologie der weissen Blutkörperchen des Hundes und Kaninchens. Skandin. Arch. f. Physiol., 1900, X, 37.
52. Thoma, R.: Lehrbuch der pathologischen Anatomie. 1894, I, 393.
53. Türk, W.: Ueber die Regeneration des Blutes unter normalen und pathologischen Verhältnissen. Centralbl. f. allg. Path. u. path. Anat., 1908, XIX, 913.

54. Weidenreich, F.: Das Gafässsystem der menschlichen Milz. Arch. f. mikr. Anat., 1901, LVIII, 247.
55. ——— Die roten Blutkörperchen. II. Erg. d. Anat. u. Entwichlungsgesch., 1904, XIV, 345.
56. Wolff, A.: Ueber die Bedeutung der Lymphoidzelle bei der normalen Blutbildung und bei Leukämien. Ztschr. f. klin. Med., 1902, XLV, 385.
57. Thayer, W. S.: Amœbic movements in Megaloblasts. Arch. Int. Med., 1911, VII, 223.



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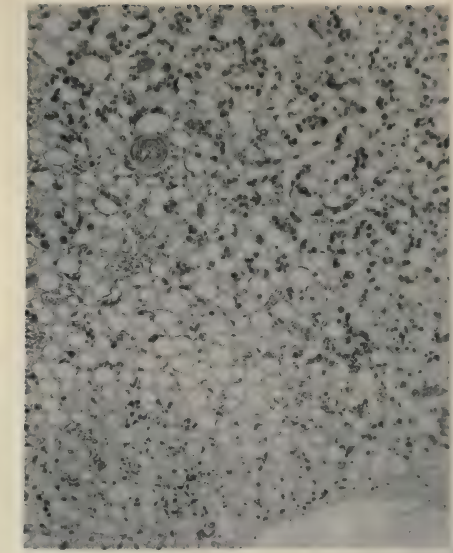

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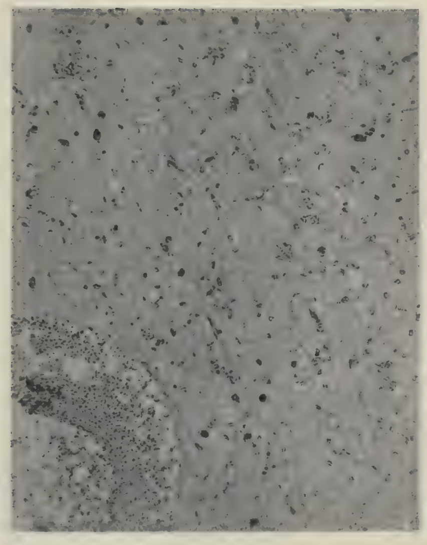

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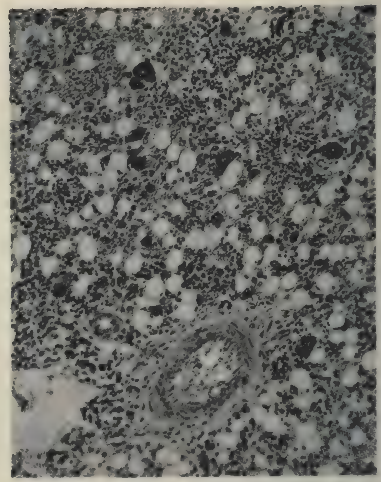

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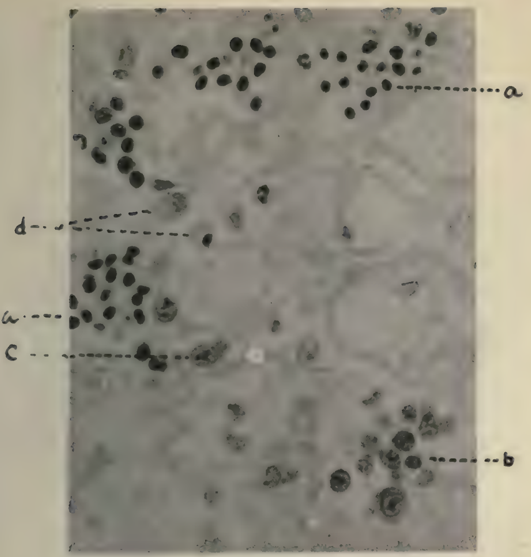

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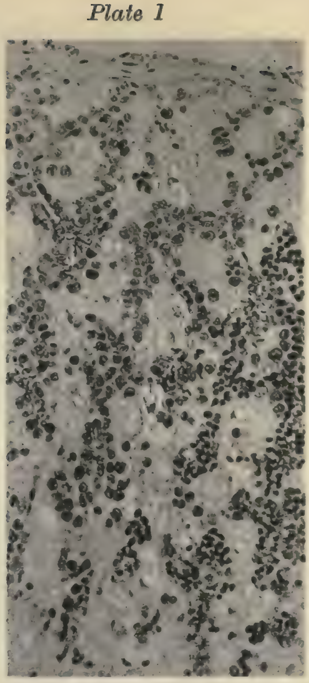

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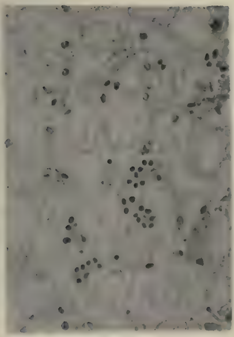

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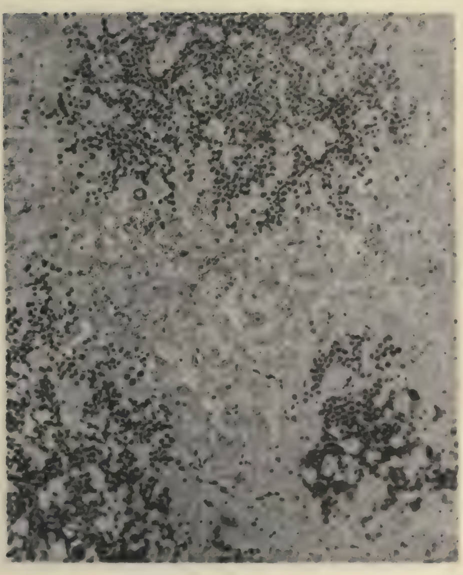

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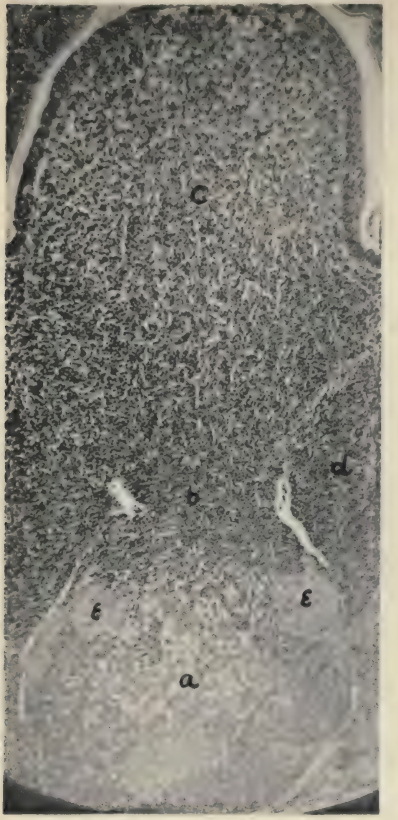

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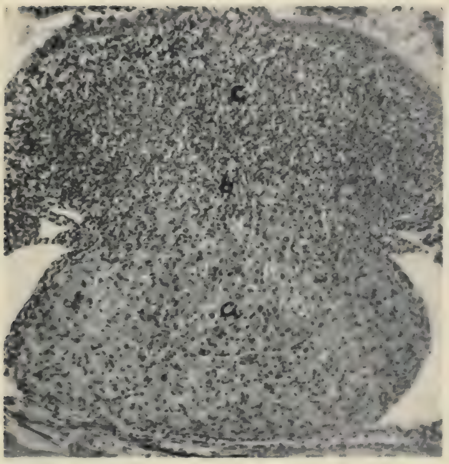

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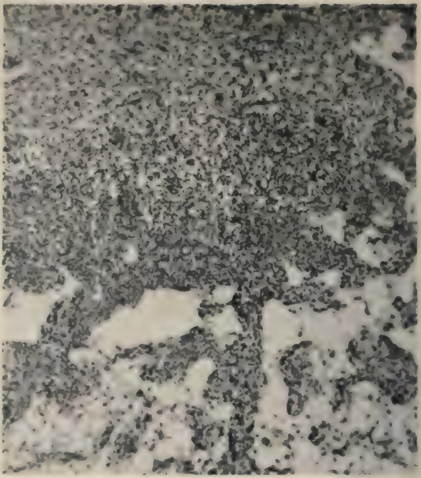

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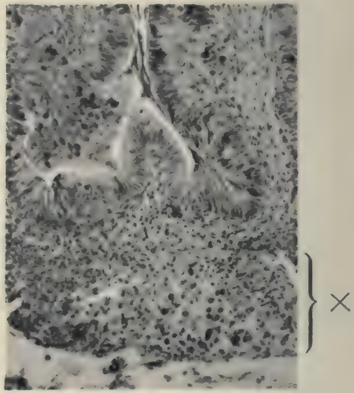

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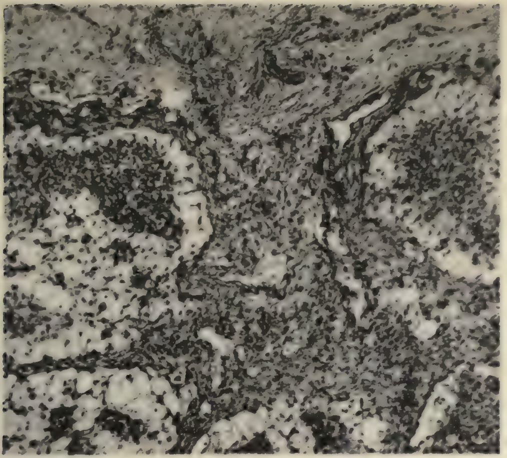

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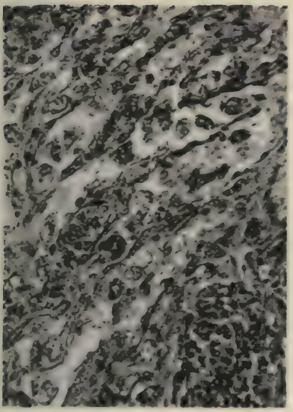

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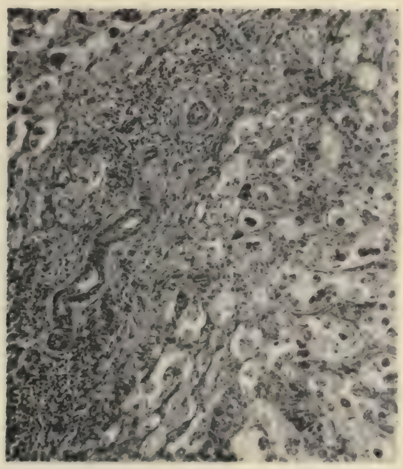

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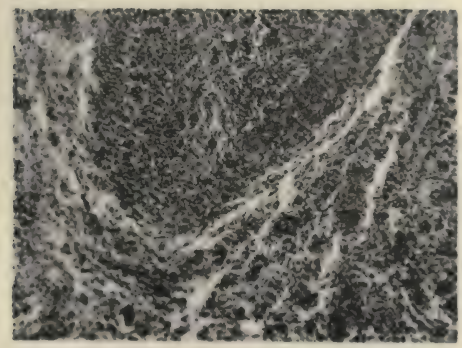

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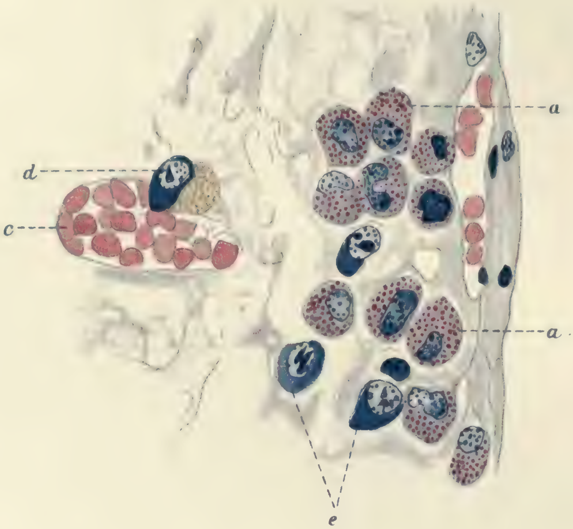

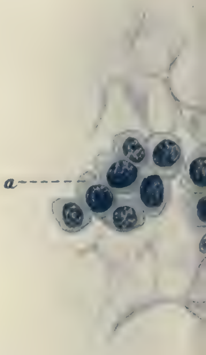

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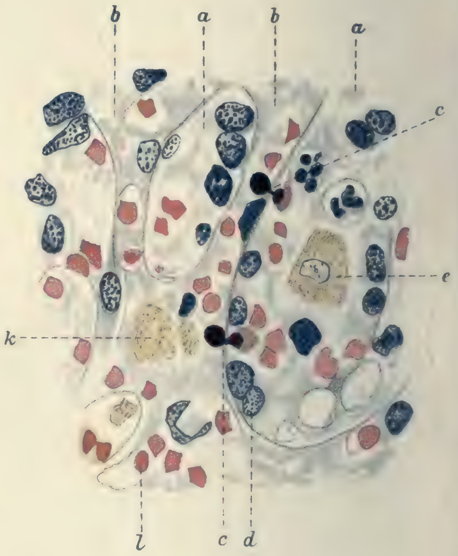

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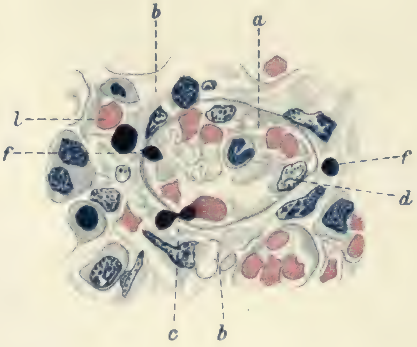

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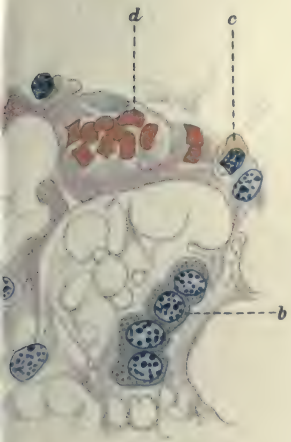

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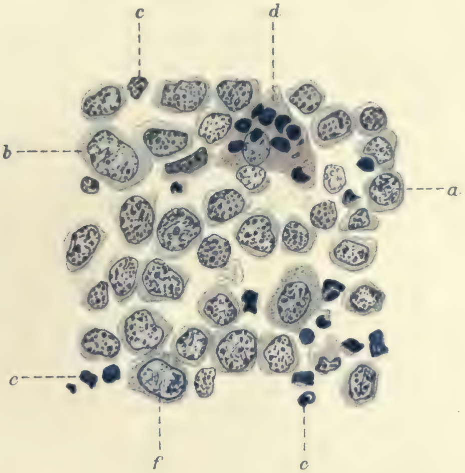

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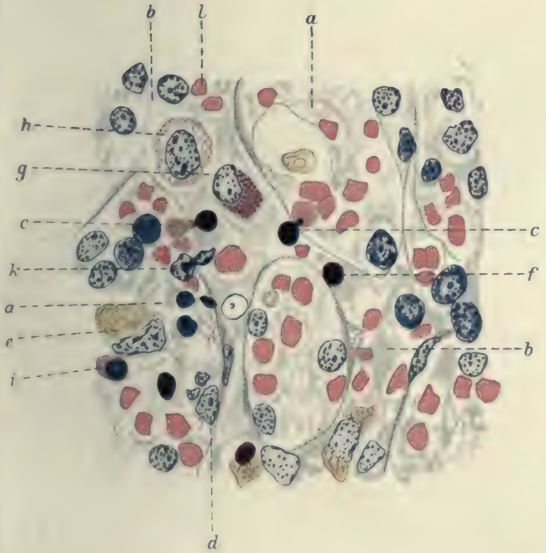

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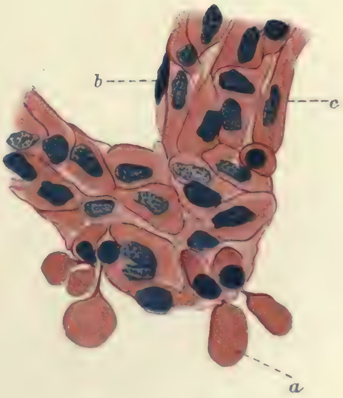

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PRIMARY CARCINOMA OF THE LIVER.

By **M. C. WINTERNITZ, M. D.,**
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The rarity of primary epithelial tumors of the liver limits their practical interest, and at the same time renders the solution of the many academic problems the more difficult. The situation might be briefly stated as follows: Epithelial new growths of the liver may, of course, arise either from the smaller bile ducts or from the liver cells. The differentiation between these two groups has offered considerable difficulty and is complicated by the possible relation between newly formed bile ducts and regeneration of the liver. While these tumors may arise in an otherwise healthy organ, their very frequent occurrence with other pathological changes in the liver, such as cirrhosis and different forms of chronic inflammatory processes, has suggested a causative relation between these conditions which is of the broadest interest in relation to tumor formation. Their simultaneous occurrence with these processes naturally connected the tumor formation with the nodular, regeneratory hyperplasias so often found in liver cirrhosis, and the similarity between these hyperplastic nodules and benign adenomata of the liver has stimulated interest in the theories concerning the relation between the regenerative hyperplasias, the adenomata, and the true cancers. Again the appearance of multiple nodules in the liver has suggested that in many instances the tumor may be multicentric in origin. It is further supposed by some observers that the subsequent development of a tumor is not only maintained by autogenous growth, but by an actual metamorphosis of liver cells into tumor cells. The early invasion of blood vessels by the malignant tumor has been repeatedly observed, but only a few observers have emphasized this finding as a possible means of explaining the apparent multicentric origin of the growth by early metastases. Finally, despite the vascular invasion there is usually an absence of extensive extra-hepatic metastases.

Needless to say, the many problems associated with the study of primary epithelial neoplasms of the liver have created considerable interest in the subject, despite the rarity of their occurrence.

The object of this paper is not to give a detailed report of the literature but to briefly summarize the various views, before describing a number of cases which seem to bring positive evidence in favor of certain views that simplify the conception of the process.

General Considerations.

Occurrence.—The oft-quoted statistics of Hansemann[1] emphasize the rarity of the condition. Out of 258 cases of cancer of the liver he found only 4 instances where the tumor was primary in this organ. Goldzieher and v. Bokay[2] say that while Orth's statistics show the absolute occurrence of primary cancer of the liver to be only 0.028 per cent, and that the combined statistics of v. Hansemann and Rindfleish increases this to 0.05 per cent, they find 18 instances in 6000 autopsies or .3 per cent at Budapest (1904-08).

Age and Sex.—The following tables copied from a recent article by Yamagiwa[3] may be utilized to indicate the occurrence of primary cancer of the liver in regard to age and sex:

Age.	Liver Cell Cancer.		Bile Duct Cancer.	
	Eggel.	Yamagiwa.	Eggel.	Yamagiwa.
1-10 years	1	2	1	0
11-20 years	2	1	0	0
21-30 years	7	2	2	0
31-40 years	12	5	2	0
41-50 years	13	2	2	3
51-60 years	28	9	1	4
61-70 years	22	0	4	1
Over 70 years	8	0	1	0
Not indicated	0	6	0	7

	Liver Cell Cancer.		Bile Duct Cancer.	
	Male.	Female.	Male.	Female.
Yamagiwa	17 or 80.95%	4 or 9.5%	4 or 50%	4 or 50%
Eggel	65 or 68.4 %	30 or 31.6%	6 or 42.9%	8 or 57.1%

Clinical Characteristics.—Hanot and Gilbert's[4] idea that it was possible to differentiate clinically cancers arising from the smaller bile ducts from those arising from the liver cells was not substantiated by subsequent observers (Karsner[5]). The condition is often not diagnosed. In the majority of cases no definite clinical symptoms point to the presence of the tumor. Vague gastro-intestinal symptoms like those of early cirrhosis are followed by more marked digestive disturbances. These may be associated with ascites, œdema of the extremities, splenic tumor, cachexia, etc., all referable to a cirrhosis. One may think of a tumor added to this if nodules of a different character are palpable on the liver or if metastases occur in accessible parts, which is most rare. Its presence naturally accentuates the course of the cirrhosis and so a rapid clinical course may be of aid in the diagnosis.

Historical.—The history of primary cancer of the liver is recent. The literature of the middle third of the 19th century contains many reports concerning epithelial tumors which were thought to arise in the liver, but most of these were subsequently demonstrated to be metastases from some obscure primary growth. No doubt examples of primary cancer of the liver are included among the early reports, but it is impossible to cull them out of the mass on account of the meagerly detailed reports.

With the teachings of Virchow, it became well known that the liver formed a very splendid soil for the localization of secondary tumors, and that metastases from very small primary growths in the mammæ, stomach, lungs, etc., might grow to enormous size in the liver. This knowledge produced such a strong reaction that it required a number of brilliant researches to establish the fact that there actually was such a thing as a primary cancer arising in the liver. It is Hansemann's [l.c.] belief that the majority of reported instances since 1870 are reliable.

However, when Kelsch and Kiener[6] in 1876 reported their two cases of primary adenoma of the liver, they were only able to find one other definite instance in the literature. Sabourin[7] then added four cases and these were soon followed by many others. The cases described were similar in so many respects that in 1888 Hanot and Gilbert [l.c.] included them as an especial type of epithelial neoplasm of the liver. They subdivided these into three groups according to their macroscopic appearance, namely, *cancer massif,* which appears as one large nodule with or without smaller ones at its periphery; *cancer nodulaire* in which numerous unequal sized nodules are scattered throughout the entire organ; and *cancer avec cirrose.* Microscopically they considered that the first two groups were almost always alveolar in structure while the cancer with cirrhosis was usually trabecular.

The subsequent development of this subject is based upon the fundamental work of Hanot and Gilbert,[l.c.] but, before entering further upon the classification and differentiation of these neoplasms, it will be necessary to correlate the various terms that have been used in connection with them throughout the literature.

An adenoma is a benign glandular proliferation in which the structure of the gland from which it arises is still definitely distinguishable. Adenomata of the liver acini may appear in normal or cirrhotic livers. They form single or multiple white, grayish-white, grayish-yellow, brownish or reddish nodules composed either of tortuous or branching ducts, or columns of liver cells which, however, are not divided into lobules. The smaller adenomata have no capsule while the larger ones may be surrounded by connective tissue. These latter proliferations of liver cells may be indistinguishable on the one hand from nodular hyperplasias, and on the other they may merge by imperceptible transitions into true cancers.

For example, a tumor with all of the characteristics of a benign adenoma, encapsulated or not as the case may be, and only distinguished from the normal liver tissue by a slightly different color and a lack of lobulation, may break into a blood vessel and form metastases within the liver or even elsewhere, so that its malignant nature is manifest. At the same time its regular trabecular nature is altered slightly, though essentially the tumor resembles the hepatic parenchyma and would certainly be correctly called an adenoma, were it not for the decided invasive and disseminating powers it displays. In fact, so little was known regarding these tumors that a sharp differentiation of them could not be expected. That this was true even as late as 1894 was recognized by v. Heukelom.[8] He says that no sharp line can be drawn between the liver adenoma and the true cancer, and that he was impressed with the malignant nature of many of these neoplasms on account of the tremendous number of instances where the tumor invaded the blood vessels.

This malignant tumor is called by many of the early French writers simply "adenoma" or "multiple adenoma" (Kelsch and Keiner,[l.c.] Marckwald,[9] etc.). Frohman,[10] on the other hand, speaks of them as "multiple malignant adenomata." Ribbert[11] alone has continued to apply the name "malignant adenoma" to the malignant tumor arising from the liver cells, and in his latest writings uses this term to distinguish the above tumor from what he speaks of as the true cancer arising from the bile ducts.

On the other hand, since Hanot and Gilbert[l.c.] included the above tumors among the cancers of the liver it has been called simply "primary cancer" by most French writers as well as others.

Still a third term is employed to designate this tumor. Siegenbeck von Heukelom l.c. preferred "adenocarcinoma," and his selection was adopted by Wegelin,[12] who believed this the more applicable term, since it refers to the similarity of the tumor tissue to liver tissue and indicates at the same time its malignant nature.

The further development of the nomenclature has been dependent upon the various classifications suggested. Hanot and Gilbert's division into *cancer massif, cancer nodulaire,* and *cancer avec cirrose* will be recalled. The greater frequency of the cancer with cirrhosis caused it to overshadow the other types of epithelial neoplasm. The remarkable coincidence of a liver with cirrhosis and neoplasm, two cardinal points of significance in the study of these cases, thus became conspicuous. The malignant tumor, of course, was of the nature of the "malignant adenoma" of Frohman,l.c. Ribbert,l.c. etc., or the "adenocarcinoma" of v. Heukelom,l.c. Wegelin,l.c. etc. The term cancer with cirrhosis has proven unfortunate. On the one hand instances have been included in this group irrespective of the appearance of the tumor, because of the cirrhosis, and on the other hand, tumors of the same gross and histological structure have been excluded, because the cirrhosis was lacking. v. Heukelom was the first to point this out, and concluded from a study of a multitude of cases that the group of cancers with cirrhosis must be greatly broadened so as to include not only those malignant tumors which had a pure adenomatous structure, but also other types of epithelial growth some of which tended towards the adenomatous structure. While this was in part correct, it proved a source of confusion inasmuch as it allowed those cancers arising from the bile ducts, which might here and there show an adenomatous structure, to be included in this group.

Ziegler[13] adopted this classification of Hanot and Gilbert. He, however, included a fourth group which is of interest since analogous instances could not be found in the literature by Eggel,[14] and which the latter, therefore omitted from his classification. This form Ziegler described as follows: The point of origin of the tumor is not definite. It spreads through the portal veins and finally involves the entire liver tissue. The development of cancer cells in the capillaries of the acini compress the liver cells which finally disappear entirely by atrophy. As the liver cells disappear the tissue contracts and causes an uneven surface similar to a cirrhotic liver. The cancer tissue is white and in this way is easily differentiated from the reddish brown or green liver tissue. As will be seen, this fourth group described by Ziegler is of interest in the light of subsequent work.

Needless to say such an arbitrary division was futile, and as Eggel l.c. pointed out Hanot and Gilbert l.c. could not conform to this classification, and included instances of *cancer massif* and *cancer nodulaire* among their examples of *cancer avec cirrose.*

Eggel then attempted a classification on much the same basis. He advanced a step, however, inasmuch as he followed the example of various authors and substituted the term "diffuse cancer" for "cancer with cirrhosis." This was necessary, since he found both nodular and massive cancers occurring either in normal or in cirrhotic livers. Eggel further attempted to differentiate more clearly the cases described in the literature into those derived from the liver cells, and those derived from the bile ducts. He divided each of these groups into two forms, the "carcinoma solidum" and the "carcinoma adenomatosum," terms which are only of passing interest. It must be noted, however, that the nodular cancer whether derived from bile duct or liver cell was the most frequent. The massive cancer was much rarer while the diffuse form was rarest of all. It always had an adenomatous structure and never arose from the bile ducts.

A much more logical basis for the designation and classification of these tumors is the one suggested by Goldzieher and v. Bokay.l.c. They attempted to divide the primary cancers of the liver into two main groups: 1. Those derived from the small bile ducts or "carcinoma cholangiocellulare" and those derived from liver cells "carcinoma hepatocellulare." Ribbert l.c. accepts these latter terms and Yamagiwa l.c. suggests a slight modification, calling the two types "cholangioma" and "hepatoma" respectively.

Histogenesis.—Ribbert l.c. is correct in saying there is no secure basis for the histogenetic differentiation of liver cancer, since the first stages in the process have not been observed. As a consequence many methods have been suggested with this differentiation in view. Certain of these tumors are bile stained. This may not only be true for the intrahepatic nodules, but also for the metastases. Such cases are included in Eggel's l.c. collection, and typical instances have been recorded by Wegelin,l.c. etc. Ribbert l.c. uses this as a differential point and says that the malignant adenomata of the liver, which he considers to be derived from the liver cells, as has been indicated, are usually colored by bile pigment within the cells of the tumor. This simple division is not absolute. On the one hand, the anaplasia characteristic of tumor cells is bound to result in a loss of the more specific functions, and, in certain instances, at least, this manifests itself in the formation of liver cell tumors in which no bile pigment occurs. On the other hand, tumors arising from the smaller bile ducts may contain bile. Examples of these have been reported by Herxheimer[15] and Loehlein.[16] The source of the bile in these bile duct tumors is disputed. While Loehlein considers that Herxheimer and others have proven that tumor cells derived from the epithelium of the bile ducts may secrete bile, still he believes that in his case the bile may have been absorbed from the surrounding liver tissue by the tumor, and simply retained. He arrives at this conclusion because there were many apparent communications between the proliferated bile ducts in the interacinar septa and the tumor nodules.

Wegelin[l.c.] also thinks that the liver cell cancer nodules communicate with small bile ducts, and would explain their very icteric appearance in some cases as a result of lack of sufficient communication with the bile capillaries.

The gross microscopical differentiation of these tumors into trabecular and alveolar (Ribbert) or solid and adenomatous (Eggel) is of relatively little assistance. Eggel lays great stress upon the histology of the tumor cells themselves. The tumor cells derived from the liver parenchyma vary somewhat from normal liver cells. They frequently have several nuclei which are usually larger and richer in chromatin than normal liver cell nuclei. The cells themselves are usually polygonal or cuboidal and may be larger or smaller than liver cells; their protoplasm is as a rule less granular and may contain bile pigment. The tumor cells arising from the smaller bile ducts are very similar to the normal lining epithelium of these ducts. They are more or less cylindrical with clear, non-granular protoplasm and irregular nuclei.

The appearance of the cells, as well as their coarser microscopical structure, is of limited value. The cells of the two classes of tumors may approach each other in appearance, and may have either tubular or trabecular arrangement. Orth, for instance, described a benign liver cell adenoma which had given rise to duct-like structures. He concluded that the presence of duct-like structures did not offer satisfactory proof of the origin of the tumor from bile ducts. This strengthened the current opinion that most of the malignant tumors of the liver were derived from the liver parenchyma. Fischer,[17] Herxheimer,[l.c.] etc., have taken the opposite view, the former actually going so far as to consider all of the malignant tumors of the liver, which showed duct-like structures, to be derived from the bile passages. Wegelin has recently put Fischer's contention to test in an interesting example of a liver cell carcinoma, and found it lacking. Herxheimer observed a case of diffuse cancer associated with hypertrophic liver cirrhosis. The tumor was pigmented, had a tubulo-adenomatous structure with high cylindrical epithelium similar to the epithelium of the bile passages, and contained bile and desquamated bile-stained epithelial cells in the lumina. Herxheimer considered this tumor to be derived from the bile passages, and found fifty-three similar examples in the literature which, with few exceptions, had been considered as arising from the liver cells. As a result of his analysis, Herxheimer emphasized the difficulty in determining the actual origin of the individual tumors, and while he did not deny the possibility of tubular structures being formed by liver cell cancers still he considered it probable that many cancers described as arising from liver cells actually originate in the smaller bile ducts. This conclusion is based partly upon the opinion that it is less likely for liver cells to form cylindrical cells than for the bile duct epithelium to form cells similar to liver cells.

With the criteria concerning the histogenesis of these tumors so indefinite, any new suggestion which might be of help must be welcomed. Wegelin's[l.c.] declaration, that in general the stroma offers a ready means of differentiating between bile duct and liver cell cancers, was propitious. He concluded that the liver cell cancer has a stroma composed only of a network of capillaries, while the stroma of the bile duct cancer is composed of an alveolar forming connective tissue. This is absolutely in accord with Dibbelt's[18] view expressed two years earlier. He says the malignant adenoma is composed of proliferated liver cell derivatives and blood vessels, in contradistinction to the bile duct cancer, in which the connective tissue is also involved in the tumor formation. These observations are the more worthy of attention since they have been independently noted and very strongly emphasized by Yamagiwa[l.c.] and his co-workers. Yamagiwa further states that the many pictures found in the study of liver cell cancers are always distinguishable from those of the bile duct cancer, since the latter never have a stroma composed only of capillaries. The many apparent transitions between these two classes of tumors, Yamagiwa says, may be explained by the increasing anaplasia of the tumor cells associated with the increasing energy of the growth. The result is a loss of the trabecular arrangement of the tumor cells which become irregularly heaped up or form alveoli. The resemblance of the tumor cells to the liver cells decreases and the capacity to secrete bile is largely lost. The relation of the liver cells to the capillaries is the property preserved for the longest time by the tumor. The tumor apparently has the power to stimulate the endothelium of the vessels in which they lodge to the formation of new capillaries, similar in their arrangement to the interacinar capillaries of the liver lobule. This capillary net, always to be found throughout the greater part of a liver cell cancer, may be replaced in localized areas by new-formed connective tissue, as in diffuse interstitial hepatitis. Associated with this, the presence of duct-like lumina, round, slit-like, or cystic in form, has been the source of the confusion concerning the separation of the liver cell tumor from those arising from bile ducts. The lumina may contain bile or detritus and are surrounded by one or many layers of cylindrical, cuboidal or polyhedral cells. These duct-like structures, however, are usually short. They are considered by Yamagiwa and his co-workers as a type of retention cyst, arising from the intercellular bile capillaries. v. Heukelom [l.c.] and Wegelin [l.c.] consider them as imitations of bile passages. The "rosette" forms, emphasized by Goldzieher and v. Bokay,[l.c.] which consist of many rows of cells arranged with their long axis perpendicular to the long axis of the lumen which they surround, Yamagiwa explains as a *Rückschlag* that is a return to forms assumed by the liver cells in the course of the embryonic development of the liver.

To sum up: The malignant epithelial tumors of the liver may be divided into those that arise from the bile ducts and those that arise from the liver cells. The occurrence of bile pigment is only of relative value in differentiating these groups, for while the bile stained nodules are usually derived from liver cells, tumors arising from small bile ducts may also have bile pigment within their lumina. They may be differentiated microscopically by the following characteristics: First, their tendency to conform to the structure of the tissue from which they arise, the bile duct cancers often forming tubulo-adenomatous, and the liver cell cancers trabecular structures; second, the conformity of the cells to the matrix type cell. The bile duct cancer cell is cuboidal or cylindrical with a clear protoplasm, &c.; the liver cell cancer polygonal or polyhedral with a granular protoplasm and occasionally containing bile pigment; third, the bile duct cancer always has a connective tissue stroma which divides it into alveoli, the liver cell cancer has a capillary stroma. Through anaplasia the liver cell cancer may assume a tubular structure in localized areas.

Relation to Cirrhosis.—The simultaneous occurrence of primary cancer and cirrhosis of the liver was so constant that as early as 1884 Cornil and Ranvier (*Manuel d'histologie pathologique*) placed the so-called liver adenoma directly after their discussion of cirrhosis. They considered these processes to be intimately associated, and, in view of recent investigations, believed the so-called adenomata to be simply a complication of the cirrhosis.

The frequency of the occurrence of cirrhosis with cancer may be illustrated by the following table:

LIVER CELL CANCER.

	No. Cases.	With Cirrhosis.	Without Cirrhosis.
Eggel	66	86.4%	13.6%
Goldzieher and Bokay .	14	100.0%	0
Yamagiwa	27	74.75%	25.25%

BILE DUCT CANCER.

	No. Cases.	With Cirrhosis.	Without Cirrhosis.
Eggel	8	62.5%	37.5%
Goldzieher and Bokay...	7	42.8%	57.2%
Yamagiwa	15	46.7%	53.32%

This table is of interest, since it points out first what a large number of cases of cancer of the liver are associated with cirrhosis, and second, that cirrhosis is much more frequently associated with cancers arising from the liver cells than with those arising from the duct epithelium.

If the cirrhosis be analyzed it will be seen that, while the larger number show simple types of annular cirrhosis, other types are not infrequent. In the series of Yamagiwa,l.c. for example, there were two cases of syphilitic cirrhosis, two consequent upon chronic passive congestion, and one, the result of emboli of Schistosomum eggs. Moreover, Bamberg, Dibbelt, Loehlein, Necker, etc., have reported the occurrence of cancer associated with echinococcus cysts of the liver. It seems, therefore, that cancer of the liver may be associated with any disease of this organ where there is regeneration following an injury.

Every possible hypothesis regarding the relation of the cirrhosis to the tumor formation has been advanced. First, that the two processes were entirely independent. This theory was held by Kelsch and Kiener,[l.c.] who, however, had very little data from which to draw conclusions and later by Frohman,[l.c.] who arrived at this opinion because the most cirrhotic areas in his preparations were free of tumor. Second, that the two processes result from the same causative factor. In many instances, the causative factor in the cirrhosis such as syphilis, parasites, etc., is known, and these could hardly be considered as etiological agents in the formation of cancer. Third, that the cirrhosis is secondary to the tumor formation. Marckwald,[l.c.] for instance, suggests that the irritation of the tumor development, even in those parts of the liver uninvolved by the growth, may lead to cirrhosis. This has no foundation, since similar tumors may occur without cirrhosis. However, the tumor nodules may cause a local proliferation of connective tissue in their vicinity, as pointed out by Wegelin.[l.c.] More than this, with extensive infiltration of the growth into the capillaries, atrophy and necrosis of the liver cells may result, which might be conceived to be associated with condensation and new formation of connective tissue; so that at an advanced stage it would be difficult to say absolutely whether or not there had been a cirrhosis preceding the cancer formation. This must be true in such cases as are included in the fourth group described by Ziegler.[l.c.] Nevertheless, the latter group must be very small as a review of the literature indicates. Fourth, in the vast majority of cases the cirrhosis precedes the cancer and is the direct cause of the neoplastic formation. This theory was first advanced by Sabourin.[l.c.] Schmieden[19] went still further, and regarded the hyperplastic liver cell islands which occur in cirrhosis as the precancerous stage.

It is not necessary to detail this conception or its development here, since it is so well known and may be found in most of the later papers on primary cancer of the liver (Eggel,[l.c.] Theodorow,[20] Wegelin,[l.c.] Loehlein,[l.c.] Goldzieher and v. Bokay,[l.c.] Yamagiwa,[l.c.] etc.). Suffice it to say that while Ribbert's[l.c.] theory, that the cancer arises from liver cells displaced and surrounded by cirrhotic connective tissue, seems to be particularly applicable in this relation, the majority of authors do not uphold it, but lean rather to the following conception: As a result of injury there is destruction of liver tissue which is followed by fibrosis and regeneration. This regeneration results in the production of hyperplastic nodules of liver cells and bile duct like structures—things that may be found in any cirrhotic liver. These products of regeneration may be indistinguishable from true adenomata, and, were it not for the cirrhosis which is sufficient to explain their occurrence, would be called adenomata. As a result of further injury of the same character, the necrosis and regeneration continue, the cells gradually lose their function and following Weigert's conception, through a proliferation exceeding its goal, become cancerous.

This hypothesis may further be utilized to explain the relatively greater frequency of liver cell cancers with cirrhosis than bile duct cancers with cirrhosis. The regeneratory powers of these structures have been determined by the experimental work of Podwyssoski, etc., and it has been demonstrated that after injury to the liver, the connective tissue, the liver cells and the bile ducts participate in the repair. The liver cells are, however, much more active than the bile ducts. Therefore, it may be concluded that they have a greater proliferative capacity, and are as a result more often stimulated to vegetative growth or cancer formation.

Mode of Growth.—The mode of growth of these tumors is still unsettled. From the very beginning it was generally conceded that each one of the innumerable tumor nodules arose in the place where it occurred, from the pre-existing liver cells in that area. This idea was supported by the transition pictures between liver and tumor cells which were described as occurring at the edge of the smaller tumor nodules. As Hansemann[l.c.] points out Schuppel[21] described these transitions as early as 1878, and his observation has been repeatedly confirmed. The most detailed and careful descriptions and illustrations of this transition were made by v. Heukelom.[l.c.] He showed not only that the columns of liver cells were, in many instances, directly continuous with columns of tumor cells but that frequently the liver capillaries were directly continuous with the tumor capillaries. The transition of liver cells to tumor cells occurs according to v. Heukelom in the following manner: The liver cells lose their peculiar light grayish-brown color and their protoplasm becomes clear and free of pigment granules, then the protoplasm becomes coarsely granular and shows vacuolar and fatty areas. The nuclear changes are still more striking; the nuclei become larger and polymorphous and contain more chromatin. The nucleoli become more conspicuous and may be increased in number. The changes in the nuclei may occur in normal cells, but the changes in the protoplasm never occur without the nuclear changes, and v. Heukelom therefore considers that the nuclear changes precede those in the protoplasm. He comes to the conclusion that cancer of the liver is multicentric in origin and that there is a progressive metamorphosis of liver cells to tumor cells at the periphery of the growth, as described by Waldeyer in skin cancer and Hauser in stomach cancer. Miss Catherine Travis, in an article published in 1902 from this laboratory, agreed with v. Heukelom's views absolutely.

Heussi,[22] a pupil of Ribbert, described an instance of carcinoma of the liver in which he had observed the above pictures described by v. Heukelom. By means of special stains (orange G) he could easily distinguish the two types of cells and found that the liver cells and tumor cells were sharply separated. He concluded that the apparent connection between tumor cells and liver cells was a sort of artifact brought about by the tumor cells growing between the capillaries and destroying the liver cells. The same process was described by Ziegler[l.c.] as noted above in his fourth type of cancer of the liver. Ribbert,[l.c.] Herxheimer,[l.c.] and Fischer[l.c.] among others adopted Heussi's view. Ribbert even illustrated * a dent in the last liver cell caused by the convexity of the free edge of the approaching tumor cell. Wegelin[l.c.] studied these transition pictures, but even with orange G, he could not clearly differentiate liver cells from tumor cells in some instances. He, however, does not consider them actual transitions since similar pictures occurred, not only at the edge of the nodule but even in their centers. He demonstrated these to be actually in the center of tumor nodules, and not on the edge, by serial sections. He concluded that these central cells are tumor cells which have preserved a greater similarity to liver cells, and draws the same deduction for the so-called transitions at the periphery. Eggel[l.c.] says, in this connection, that the significance of the apparent transitions has been greatly overvalued as is evident from observations of Ribbert, Perl, Naunyn and Schmidt, who describe similar pictures occurring in metastatic growths where the secondary nature of the cancer is unquestionable. He also comments upon the absence of nuclear figures in these transitions. v. Heukelom[l.c.] remarks upon their absence, and Frohman[l.c.] finds that they only occurred in well preserved liver lobules and not at the border of the tumor. On the other hand, mitoses

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* Cf. Das Karzinom. Fig. 378, p. 446.

have been repeatedly observed in the tumor cells which Eggel considers as positive evidence for autogenous as against appositional growth. He further states that, through the contact of liver cells and tumor cells, pictures closely simulating transitions are produced. The possibility of mistaking these is dependent upon the fact, that with our present methods, it is impossible to find a means to specifically differentiate these cells. Wegelin's l.c. suggestion is of interest in connection with the above statement.

Adler differentiates two types of cells in the normal liver lobule by means of osmium stained preparations. In the fœtal and infant liver many light, only slightly granular, fat-free cells without any brownish color occur. These Adler thinks are younger forms. In the adult liver only dark brown, densely granular, fat-containing cells occur which he thinks are older forms. Wegelin suggests that an analogous differentiation possibly occurs in cancer. This he thinks the more plausible since the larger nodules, evidently the older, are composed of darker cells while the smaller, younger ones consist of paler cells.

With all of the facts of the controversy in mind Goldzieher and v. Bokay l.c. still emphasize the transition of liver cells to cancer cells, which seems to them to be demonstrable in their 12th, 15th and 20th cases. Yamagiwa,l.c. in his abstract of his assistant Kika's report, says that, in the majority of cases, transitions could not be found. He, however, was convinced of their occurrence in one instance, and concludes, that while they are most rare, they can occasionally be seen, not at the periphery but in the center of the primary nodule, or in young nodules in instances of multiple origin. This opinion is of interest in relation to Wegelin's observation above quoted.

Evidently there is no harmony in the views concerning the so-called transitions. This much may be said, however, that subsequent work has in no way corroborated their very frequent occurrence, that they are denied by many, and are only found as very rare occurrences by those that do describe them.

Concerning the metamorphosis of liver cells to tumor cells, there is an equal lack of agreement. Eggel l.c. refutes it entirely and considers the growth entirely autogenous. Goldzieher and v. Bokay l.c. also say that appositional growth does not occur. Wegelin l.c. is more conservative. He says that while the possibility of a transition of liver cells to tumor cells is not to be negated with certainty, still the tumor does not enlarge to any extent by appositional growth.

Are primary cancers of the liver unicentric or multicentric in origin? In general it may be said that those observers who emphasize the importance of the above described transitions at the periphery of the tumor nodule believe in the multicentric origin of the cancer. This, for instance, is v. Heukelom's conception and following his idea, Miss Travis[23] believes that in her one example there were multiple primary tumors. This same conclusion is reached by Loehlein[l.c.] for his second case. Goldzieher and v. Bokay[l.c.] who, it will be recalled, believe the transitions to occur, state positively that they believe all primary cancers of the liver are multicentric in origin. Yamagiwa[l.c.] summarizing Kika's paper says that of 30 cases, 17 arising from the liver cells and 7 from the bile ducts were multicentric. He concludes that from the standpoint of their genesis it is probable that every primary cancer of the liver is multicentric in origin, for both forms of cancer of the liver arise, either on the basis of a regeneratory hyperplasia of liver cells, or inflammatory hyperplasia of bile ducts. These hyperplasias, Yamagiwa says, occur in many neighboring areas, *i. e.,* are multicentric and not in a single circumscribed area, etc., *i. e.,* are not unicentric.

The unicentric origin of cancer of the liver has been particularly advocated by Ribbert[l.c.] and his pupil Heussi.[l.c.] In his book (Das Karzinom, 1911), Ribbert says that primary cancer of the liver is not necessarily multiple, it may form one large nodule and only very late form small metastases. As a rule, however, the liver contains many varying sized nodules, but the multiplicity is not primary. Even the smallest tumors are circumscribed and must have arisen from dislodged cells and each group of smaller nodules may be recognized as metastases, and traced back until a primary nodule is reached. The secondary growths are brought about through the invasion of the portal vein by the primary tumor. Elsewhere, his view is more clearly expressed. He says that most of the nodules are sections of tumor cords which represent the portal vein dilated and filled with tumor masses. It is well known, Ribbert continues, that this tumor by predilection invades the liver veins, most often the portal, where it grows as well with as against the current. In numerous instances, he says, it was possible to pull the tumor thrombus out of the branched bed of the portal vein, in cast-like form, when this was found to compose by far the greater mass of the tumor.

In other cases, according to Ribbert, the nodules are either to a great extent or entirely isolated, but even then they are not multiple primary tumors if the portal vein has been invaded at any point, as the blood rushing through will break off small particles and carry them further to form secondary nodules.

This conception of the mode of dissemination of the tumor, Ribbert says, is not a new one, but it has not been sufficiently emphasized. It has been corroborated recently by Wegelin l.c. and Loehlein.l.c. That Sternberg also leans to this opinion is evident from his statement in the last edition of Aschoff's Pathology.

Relation to Adenomata.

After the foregoing discussion there remains little to be said concerning the origin of these tumors from benign adenomata. The consensus of opinion is that the nodular hyperplasias, which may be indistinguishable from true adenomata, are the source of the cancer. It has therefore been concluded by many that all cancers first pass through the benign or adenomatous stage.

There are, however, a small percentage of cases of primary cancer of the liver unaccompanied by cirrhosis. In this group especially the possible origin from adenomata must be considered. Ribbert considers that the cancer may occur from misplaced embryonal rests, and thinks this conclusion justified, since we recognize the occurrence of benign adenomata of the liver in early life. Many of these, he says, suggest developmental anomalies, since they have been associated with other abnormalities such as absence of the quadrate lobe (Engelhardt), etc. Yamagiwa comes to the same conclusion, inasmuch as he could collect five cases of primary liver cell cancer in children associated with an embryonic rest (*Überschüssiger Anlage des Mesenchymgewebes aus welchem auf dem metaplastischen Weg Knochen, Knorpelgewebe sich entwickelt hat*).

These embryonic rests both Ribbert and Yamagiwa consider sufficient to account for the cases of cancer of the liver without cirrhosis. They say most cancers without cirrhosis occur in children, or in early adult life, though in some instances the embryonic rest may remain dormant until adult life and only then become malignant.

Extra-hepatic Metastases.—While these are not numerous and, as a rule, do not attain any considerable size, still Eggel,l.c. in his review of the literature, found that they occurred in 66 per cent of the 163 cases collected. and of the remainder 35 formed tumor thrombi in the large veins; the thoracic and mesenteric lymph glands are most often involved while the lungs are the next most frequent site (23 cases). Metastases are more likely to occur earlier and more frequently in cancers arising from the small bile ducts.

The only explanation of the relative infrequency of metastases is offered by Wegelin. He thinks that even in those cases without apparent metastases, tumor cells may have reached the arterioles of the lungs, where they were encapsulated or destroyed by organization and rendered harmless in this way. M. B. Schmidt has demonstrated this in cancer of the abdominal viscera.

CASES.

Case No. 1.—S. W., male, black. Medical Nos. 26659 and 27735. Patient was first admitted to the medical clinic of The Johns Hopkins Hospital December 9, 1910. At that time he complained of pain in the right chest, radiating into the back and shortness of breath. A diagnosis of mitral insufficiency was made. He remained in the hospital several weeks and left in a slightly improved condition. He was readmitted on August 4, 1911, complaining of swelling of the stomach and pain in the right side of the chest. His past history, until December, 1910, was unimportant. Since then he had suffered with dyspnœa on exertion and his sputum had been blood tinged. Two weeks before admission his abdomen became swollen. This was accompanied by abdominal pain which was exaggerated on eating. A week before admission he vomited a clot of blood which was dark red in color and quite large. He had always done hard labor and consumed considerable whiskey during the latter part of his life. There was general glandular enlargement. Heart somewhat enlarged, an apical, systolic murmur well transmitted to the axilla. Abdomen greatly distended and definite evidence of effusion in the abdominal cavity. Legs œdematous. On August 7, six and one-half liters of greenish fluid, with an albumin content of nine grams per liter, were removed from the abdominal cavity. Paracentesis was repeated on August 21 and September 7, when the fluid showed many red blood cells microscopically. After the tappings the liver was easily palpable. It had a hard edge which was palpable three fingers below the costal margin in the mammillary line. The surface was very nodular. These nodules varied from 0.5 to 2 cm. in diameter. On September 7 the scleræ became icteric. Paracentesis on September 15 yielded a blood-stained fluid and gave a positive bile reaction. The next day the patient was allowed to go home and on September 19, following a severe hematemesis, he died.

Autopsy No. 3600 performed two and a half hours after death by the author.

Anatomical Diagnosis.—Cirrhosis and cancer of the liver; invasion of the portal vein by the primary carcinoma and extension of this thrombus into the splenic and mesenteric veins; metastases to mesenteric lymph glands and lungs; hemorrhagic ascites; œsophageal varices; rupture of œsophageal varix; hemorrhage into the stomach and intestine; jaundice; chronic mitral endocarditis; dilatation of heart; chronic fibrous myocarditis; healed miliary tubercles in lungs; anemia; emaciation; œdema of extremities.

Protocol.—Body is that of a large colored man, 172 cm. in length. Rigor mortis is present. There is no lividity of the back. Scleræ are of a yellowish color. The mouth and teeth are blood stained and blood is also present over the face and chest. Abdomen is markedly distended, legs are œdematous. The skin is everywhere loose. The subcutaneous fat is very small in amount. Abdominal muscles are thin and flabby. The abdomen contains about eight liters of a markedly blood-stained fluid, otherwise the peritoneal surfaces are everywhere smooth and glistening. A tremendously enlarged, hobnail-like liver projects far below the costal margin, reaching as far as the umbilicus in the mammillary line. Several large, firm glands may be felt in the mesentery. Pleural and pericardial sacs present nothing abnormal.

Lungs: Three small nodules about 0.5 cm. in diameter are scattered through the lung tissue. These are firm, and on section have a grayish, translucent color. They are just beneath the pleural surface.

Stomach and duodenum are full of unclotted blood; œsophagus shows a few dilated varices just at the cardia. One of these projects through the mucosa and has an eroded mouth, into which a probe can be readily passed.

Veins: The splenic vein is filled with a large mass which has an opaque, yellowish appearance. The mesenteric vein is likewise occluded by a thrombus which joins the one in the splenic vein. These together fill the portal vein, which is much dilated and measures three cm. in diameter at the hilus of the liver.

Liver is enlarged, measures 32 x 24 x 15 cm.; weighs 3200 grams. The left lobe is not so much enlarged. It has a coarsely granular or hobnail surface. The nodules vary from the size of the head of a pin to 1 cm. in diameter. In some places they are incompletely fused and larger protuberances are formed. The nodules vary in color, sometimes they are quite black or grayish black, others are brown, and still others are yellowish and opaque. The capsule over the left lobe is not thickened. Hanging from the dome of the right lobe is a pendulous nodule about three cm. in its longest diameter, attached to the capsule by a delicate fibrous pedicle. To the right of this the capsule is thick and gray in color. The greater portion of the surface of the right dome is taken up by several large, soft, yellowish projections. The remainder of the surface is similar to that of the left lobe. A tranverse section was made through the liver just behind the entrance of the portal vein into the hepatic parenchyma. The liver tissue is everywhere studded with tumor nodules—the right lobe is almost entirely converted into tumor masses, and only between these and at the periphery is the liver parenchyma still visible. The liver tissue varies from a greenish brown to a deep green color. Its architecture is everywhere distorted, and, particularly at the periphery, depressed grayish areas of fibrous tissue are seen running through the liver tissue, distorting the architecture of the lobules. In the left lobe there has not been so much destruction of liver tissue. The liver tissue is much more evident and the tumor nodules fewer. The parenchyma is for the most part deep green in color. The tumor nodules vary from a grayish to a grayish-white or grayish-yellow color. The smaller ones are grayish white and semi-translucent, the larger ones have yellowish, opaque streaks running through them. These opaque areas become prominent in the largest nodules. Many of the smaller nodules are definitely circumscribed, round or oval in form. This is also true for most of the larger ones. In some places the larger nodules seem to be the result of fusion of smaller ones. On dissection it is found that a large number of these nodules are cord-like processes extending through the larger veins, and many of them can be directly traced to the large mass, occluding the portal vein at the hilus of the liver. At the edge of the left lobe, where the tumor nodules are still small, a section can be made parallel to the portal venules, and in several instances one can readily see a grayish-white opaque mass, extending as a broad line toward the capsule of the liver and giving off from either side small rounded tumor masses. The distribution of the tumor in such an area corresponds absolutely to the branching bed of the portal vein, and it is of interest to note that the development of the nodules within the liver parenchyma, even in such an area as above described, is unequal, for the nodules connected with the portal vein vary considerably in size. The mass within the larger portal vein is yellowish in color, spongy in consistence, and in many places quite friable. It has nothing to indicate any relation to a thrombus, but resembles much more a mass of necrotic tissue.

Sections were taken from numerous portions of the liver, for histological examination. The normal architecture of the liver is in many places extremely obscure, on account of the presence of larger and smaller tumor nodules, which are scattered throughout.

In one section, however, from the left lobe, just beneath the capsule, quite a large area of liver tissue is still to be seen. The capsule is somewhat thickened and shows a slight infiltration of small cells with relatively large deep staining nuclei. The capsule is very irregular, and in many places dips down into the substance of the liver, and is continuous with dense bands of fibrous tissue running through the hepatic structure. Between two such depressions, a mass of liver tissue, possibly the size of a dozen lobules may be seen on section, and in this area, aside from a thickening of the connective tissue in the periportal space, no definite evidence of cirrhosis is to be made out. Some of the bands extending in from the capsule are quite wide and obliterate the normal architecture of the lobule. As these bands of fibrous tissue are followed, larger and smaller circumscribed tumor nodules are to be found within them. In some places the tumor nodules are cut along their long axes and then are found to branch as though they were lying within the bed of a vessel.

It is worthy of note that within all of these fibrosed areas larger or smaller tumor nodules are to be found, and that between the fibrosed areas larger and smaller zones of liver tissue occur, in which the architecture is still preserved, and in which no tumor nodules are to be found. This becomes the more conspicuous where the blood vessels lying beneath a large, fibrocellular depression in the capsule, which may involve several lobules of the liver, are found occluded by a large tumor mass. The liver tissue is altered everywhere by the presence of the tumor nodules. In many places the liver columns are compressed, and show a progressive atrophy between two large nodules. In some places, in fact, the liver cells seem to have disappeared for the most part, leaving behind them only a meshwork of blood vessels and connective tissue. In some of these places the atrophy of the liver cells has been so recent that clefts still occur where the cells have disappeared, and in still other places small columns of liver cells may be found in the center of such fibrosed strands. In other areas still another type of picture is found: associated with the atrophy of the liver cells, the intralobular capillaries are so tremendously dilated that the picture of an angioma is produced in the center of each lobule.

It will thus be seen that, as a result of a compression of the hepatic tissue between tumor nodules, an atrophy of the liver cells may be produced, resulting in a secondary condensation of fibrous tissue which may produce a picture of cirrhosis. Again, as a result of the invasion of this tumor into the intralobular capillaries, pictures resembling angiomata are produced which likewise are brought about by a disappearance of the hepatic cells. In still other areas the liver cells are found to be in a poor state of preservation. Such an area is found lying just beneath the capsule and is irregularly wedge-shaped. It suggests very strongly that we are dealing here with an area of necrosis, the result of plugging of the small interlobular branches of the portal vein. This would be the third way in which fibrous tissue bands might result from the growth of the tumor, and so bring about a picture of cirrhosis.

The liver cells are sharply defined everywhere from the tumor cells. They are more regularly arranged. Their protoplasm is, as a rule, larger in proportion to the size of their nucleus than in the tumor cells, and they stain a paler grayish- or bluish-brown color. In some places they are small, atrophied or necrotic and only appear as brownish masses due to the lodgment within them of rather coarse, brown granules. In other places they are compressed and are entirely free of this pigment, while still elsewhere definite areas occur where they appear hypertrophic. Here the nuclei are larger, more deeply staining and the cell protoplasm has a clear pale blue appearance. In such areas the nuclei vary considerably in size and in chromatin content. It is not rare to find two or three nuclei in a cell or to find nuclei with more than one nucleolus. Such areas may be found in portions of the liver tissue, distant from any tumor nodule, and in certain instances, where the section has taken a good eosin stain, the protoplasm of these cells stains a delicate pink, which distinguishes them readily, if this were necessary, from the tumor cells. The variation in the pictures of the liver cells is tremendous, since throughout the section the different processes—pressure atrophy, congestion, necrosis, and condensation of fibrous tissue are occurring in different proportions.

The tumor nodule: By far the greater number of nodules, both large and small, are definitely circumscribed. They are surrounded by a connective tissue wall which resembles very closely a blood vessel. What is more, it is almost possible to predict in looking through the sections where a tumor nodule will next be found, since all of the small nodules lie in the periportal connective tissue and have next to them a bile duct and an hepatic artery. In some places, where it was attempted to cut these nodules along their long axis, it was found that they occur as long cylinders with bud-like projections, extending at indefinite intervals from their lateral margins. Sometimes the bud-like nodules have bulbous extremities.

This has emphasized the importance of the relation of the tumor nodule to the blood vessel, and to bring out still further this point a number of elastic tissue stains were made. In these latter sections the tumor nodules in many instances are characteristically outlined by a wavy blue line of elastic tissue, showing, without doubt, that the tumor nodule lies within the blood vessel. This might have been suspected from the fact that in most instances the endothelial lining of the blood vessel is still well preserved.

In other areas one cannot be so sure that the tumor nodule is confined to the blood vessel. In many areas the vessel wall is lacking, and the tumor cords extend out into the liver lobule bringing about, in some instances, pictures which might be called transitions from the liver cells to tumor cells. Instances where this mistake might be made are extremely rare, for, as a rule, a few serial sections will show that the tumor, a little further down, is confined to a vessel and only later, by its outgrowth into the capillaries of the liver, does it destroy and replace this by tumor tissue. The tumor nodules are for the most part composed of columns and solid nests of cells which, except for minor details, bear a relatively close resemblance to liver tissue. The cells are irregular, rectangular or polyhedral in shape, not as large as normal liver cells and their protoplasm stains more intensely blue. Their nuclei are about the same size as the nucleus of the normal liver cell and, except for the fact that mitoses are frequently found within them, do not present any pictures which may not be found in the normal liver cell. However, the diversity of size and amount of chromatin is much more striking in the tumor cell than in the liver cell. In the smaller solid nodules these cells are only separated from each other by very delicate capillaries, and this picture is retained throughout the section. Nowhere, even in places where alveoli and rosette like structures are found, are bands of fibrous tissue to be made out between the columns of cells.

In larger nodules it is not infrequent to find areas of necrosis. In these the protoplasm of the tumor cell first grows pale and shrivels, and the nuclei then show various stages of karyolysis and karyorhexis. The result of this necrosis may best be seen in the large tumor thrombi. These consist of a small rim of tumor tissue surrounding the vein wall with a central pink-staining core of tissue, in which no structure is to be made out, occupying by far the largest part of the lumen of the vessel. Although the liver cells are arranged in definite columns as a rule it is not uncommon to find a dilated space between such columns that resembles a lumen. These smaller dilated spaces usually lie between two cells and later appearances closely resembling bile ducts occur. A row of cells with their long axes perpendicular to the axis of the lumen are found. Not only is this formation present, but occasionally many rows of cells, with their long axes perpendicular to the long axis of the lumen, occur, producing a so-called peritheliomatous arrangement.

To summarize: The patient was a black male, aged 60. There was nothing to indicate disease of the liver in his history or on physical examination eight months before death. His present illness had only manifested itself about seven weeks before death, and the cardinal features were abdominal pain and swelling; enlarged, nodular liver; hemorrhagic ascites, and hematemesis.

At autopsy, the liver was much enlarged and had an irregular surface. On section the grayish tumor nodules were readily distinguished from the green liver parenchyma. Most of the right lobe of the liver was occupied by many nodules of varying sizes while smaller ones were scattered throughout the left lung. They were all circumscribed. The portal vein was plugged by a tumor thrombus, and many of the nodules described above were simply sections of these cords, as could be readily demonstrated by sections running through the long axis of the vessel. Metastases were found in the mesenteric lymph glands and lungs.

Microscopically, those areas of liver tissue that were not densely infiltrated with tumor nodules showed no cirrhosis. Elsewhere, however, the liver parenchyma had suffered greatly from the presence of the tumor nodules. Complete atrophy of the liver cell resulting in a condensation of the stroma and a connective tissue proliferation occurred between larger tumor nodules. In other places circulatory disturbances, due to the presence of the tumor in the veins, had brought about great congestion of the interacinar capillaries and atrophy of the liver cells. But in still other places, probably as a result of occlusion of the smallest portal vessel, necrosis of the liver cells was found. In these various ways a picture simulating a cirrhosis was produced.

The liver cells were easily distinguished from the tumor cells. Even in the hyperplastic nodules of liver tissue, the liver cells were more regular in appearance, had a greater amount of protoplasm which stained pale pink and was finely granular. In some instances the liver cells had several nuclei.

The tumor nodules were almost all definitely circumscribed and most of them were enclosed in the lumen of a blood vessel, which could be demonstrated by the endothelial and elastic tissue coats. In such areas where the above picture was not distinct, and where transitions seemed to occur, serial sections readily demonstrated the connection of the nodule to the tumor thrombus. The tumor cells were cuboidal, irregular in shape, with indefinite granules in their protoplasm, and nuclei which varied in size and chromatin content. Mitoses were not infrequent. In the larger nodules, and in the center of the tumor thrombi where the cells were not so well preserved, they became paler and larger, and their nuclei smaller and more pyknotic. In this way the tumor cells came to resemble the liver cells.

The tumor cells were arranged in nests or columns, and rarely formed duct-like structures. The stroma consisted only of a delicate capillary network.

CASE No. 2.—G. K., white male, aged 52. Medical No. 10953. Patient was admitted to the medical clinic of The Johns Hopkins Hospital February 4, 1900, complaining of swelling of the abdomen. He had suffered from gastric disturbance to a greater or less extent for 31 years. During this time he had had numerous attacks of vomiting after eating or drinking. These usually lasted from two to three days. Otherwise he had been quite well. Two weeks before admission (February 10) patient found on arising in the morning that his abdomen was greatly swollen. This same day he had abdominal pain. Early in February he had noticed some blood in his stools. On examination he was found to be a well developed, poorly nourished man with a sallow complexion. Abdomen was distended with fluid. The liver was enlarged and extended 8 cm. below the costal margin in the mammillary line. The edge was firm, the surface nodular and tender.

Autopsy No. 1533 performed 10 hours after death by Dr. Opie. *Anatomical diagnosis:* Hæmochromatosis with pigmentation of the liver, pancreas and abdominal lymph glands; cirrhosis of liver; primary carcinoma of liver; invasion of the portal vein; ascites; chronic passive congestion of the abdominal viscera; old pleural adhesions; calcified nodules in lung; adherent pericardium.

Protocol.—Body is that of a very emaciated man. The peritoneal cavity contains 700 cc. of cloudy, dirty, yellowish fluid. Everywhere ecchymoses are found over the peritoneum, and the peritoneal surface is less glistening than normal. The lower margin of the right lobe is 11 cm. from the end of the sternum, and 4.5 cm. above the umbilicus. The gall bladder is distended and projects below the surface of the liver.

The *liver* weighs 4200 grams; measures 32½ x 25½ x 13 cm. The enlargement involves both lobes, the right, however, somewhat more than the left. The surface of the organ is very irregular. Over the entire surface are nodular projections of a yellow color. These are very irregular in outline and stand out conspicuously above the general dark brown surface. Such yellow, projecting masses in the outer and posterior three-quarters of the right lobe, are in a large part continuous and form large masses between which little liver tissue is still preserved. These larger masses are seen to be rounded on section, and surrounded by a delicate fibrous tissue membrane. The tissue forming them is in general very soft and brain-like in appearance. The larger ones contain in the center firm, solid, opaque, yellow material. Throughout the organ, most numerous and most abundant in the right lobe, are tumor masses, the largest of which on section are 2 cm. in diameter. The smallest are hardly visible. The veins are distended and plugged with very soft, yellow, semi-solid material, which can be squeezed out. The portal vein is greatly distended measuring 3.5 cm. in diameter, as it enters the liver. It is filled with an opaque yellow material. A section bisecting a portal vein and its branches, in the substance of the liver, shows them to be filled with tumor material. On further dissection, it becomes evident that many of the large tumor masses, seen on section, are continuous with the mass occupying the portal veins. The hepatic veins are free. In the left lobe of the liver, the portal vein, cut longitudinally, is filled with soft material. It is very soft and is nowhere attached to the intima. In the left lobe of the liver, and in the adjacent fourth of the right lobe the tumor nodules are of smaller size (about 1 cm. in diameter) and are less abundant. The liver tissue is firm in consistence and has a homogeneous, deep golden brown color. The gall bladder is distended and measures 10 cm. in length, containing greenish-black, slightly viscid bile. The mucous membrane is aparently normal.

Microscopical notes.—The first section is free from tumor nodules. The liver tissue is involved in a marked cirrhotic process. The fibrous connective tissue is particularly marked in the periportal areas, but is not equally distributed. Smaller and larger strands of fibrous tissue are found in these zones, but a typical annular cirrhosis does not occur. In some places there is only a small increase of fibrous tissue about the portal space, while elsewhere there are huge, irregularly stellate scars devoid of liver tissue. Here and there small bands of fibrous tissue run into the lobule from the periphery and, in this way, separate smaller and larger groups of liver cells. The fibrosis is more conspicuous in sections showing tumor nodules where the liver tissue is not only disappearing as a result of the cirrhotic process, but where masses of liver tissue are greatly compressed by tumor nodules, and where local areas of congestion bring about a similar result. In a few small areas necrosis is to be seen in the liver cells. The tumor nodules are for the most part encapsulated in dense bands of fibrous tissue. At the periphery of these, remnants of compressed liver cells may still be made out. It is a simple matter to differentiate the tumor tissue from the rest of the section, it being the only tissue in which pigment is not found. Throughout the rest of the tissue, including the fibrous septa and liver cells, an abundance of brownish pigment, identified by a special staining method as hemosiderin, occurs. It appears as amorphous masses or more often as small granules of a yellow color and is particularly dense in the interacinar septa. Here it may be found within spindle cells, but as a rule it forms large clumps of a mulberry shape, and its absolute localization cannot be told. In the liver cells this pigment occurs as innumerable, fine granules, usually surrounding the nucleus, while the periphery of the cell is free. However, many cells, usually small ones, are entirely filled with the golden brown pigment, so that their nucleus is only very indistinctly visible. In the lumina of the interacinar capillaries, masses of pigment lie between the red blood cells. In the tumor nodules, despite careful search, no pigment is to be found, and here and there, where a few liver cells remain intact surrounded by a fibrous tissue band, they are apparently undergoing a compensatory hypertrophy, and are likewise either entirely free or contain only a few pigment granules. In the fibrous connective tissue, aside from the dense masses of pigment above described, occasional clumps of isolated liver cells and bile duct like structures occur. The latter are in some places very numerous, and here and there seem to have bulbous extremities full of cells resembling liver cells. In some instances these cells are pigmented, but as a rule the bile duct like structures are free of pigment. Large numbers of round cells scattered either diffusely or occurring in clumps are also found in these fibrous strands.

The tumor nodules are easily distinguishable, firstly, on account of their lack of pigment; secondly, on account of the greater affinity their cells have for hæmatoxylin; thirdly, since they are as a rule definitely encapsulated by dense fibrous tissue bands, and finally since they form arborescent, tree-like structures which simulate the branched bed of a dilated vascular trunk. That most of these nodules are definitely within a blood vessel is easily established by the elastic tissue stain, which shows many of them to have a delicate but definite elastic coat around the tumor nodule. Often the elastic stain is not necessary, since the endothelial lining of the blood vessel is still preserved. Serial sections are particularly valuable in demonstrating the relation of the smaller nodule to the larger trunks, for in some instances these smaller nodules are not entirely circumscribed, but have grown out into the interacinar tissue so that transitions from the liver cells to tumor cells seem to occur. This picture is not confusing on account of the difference in the staining reaction and the lack of pigment in the tumor nodule, and a few serial sections suffice to demonstrate the connection between these nodules and the larger masses lying within the portal vein. The tumor cells bear an extraordinary resemblance to the liver cells, both in their morphological characteristics and in their arrangement. The cells are rectangular or polygonal in shape, their protoplasm stains a pale pink and is smaller in proportion to the size of the nucleus than is usually true for liver cells. The nuclei present a variable appearance. Some are small and pyknotic, but the greater number have large, vesicular nuclei with several nucleoli. Mitoses occur in the tumor cells, but are not common. Some nuclei are exceedingly large and in still other places several nuclei may be found lying within one cell membrane. The cells are arranged in columns and are separated from each other only by a delicate capillary stroma. In some of the larger capillaries paler staining areas occur within the tumor. Here the cells are larger and bear a much closer resemblance to liver cells than the remainder of the tumor. In such areas, if these be considered liver cells, and they might be easily mistaken for such, transitions between them and the tumor cells could be readily made out and might bring about a wrong interpretation. The formation of tubular structures is rare in this case. Here and there small lumina may be found between tumor cells and occasionally these are dilated considerably to form cyst-like areas, but that they are actual dilatations within the tumor, and not part of the structure of the tumor, may be readily made out on account of the compression of the cells surrounding them. In the sections examined, the tumor nodules are everywhere well preserved. Only small areas occur where the tumor cells are beginning to show disintegration. Here the tumor cells stain and resemble in general the pale cells described in the larger blood vessels. This seems to lend evidence to the possibility that the paler cells resembling more closely the liver cells may result from local conditions of nutrition, etc.

To summarize: The patient was a white male, aged 60. His history indicated that he had suffered from a slowly progressing cirrhosis of the liver. This terminated in a rather sudden ascites which was accompanied by abdominal pain. On examination the liver was found enlarged, firm and nodular. At autopsy, the liver was much enlarged and had a very irregular surface. On section the tumor nodules were yellowish or yellowish-gray in color, and were sharply outlined from the deep golden brown liver tissue. The tumor formed large masses occupying the greater part of the right lobe. They were circumscribed and surrounded by a delicate fibrous tissue membrane. The nodules in the left lobe were smaller in size. The portal vein, and all of its branches examined, in both the right and left lobes, were filled with tumor tissue which in many places formed the nodules, seen on section. Microscopically, even in those areas where no tumor nodules occurred, there was a marked cirrhosis. In the region of the tumor nodules the fibrosis was greater, as a result of atrophy and necrosis of the liver cells. The tumor cells were easily distinguishable since they lacked the pigmentation found in the remainder of the liver tissue. The hyperplastic nodules, which occurred rather abundantly, were also either entirely free or contained only a small amount of pigment, but their cells stained so differently that no confusion was possible between them and the tumor cells. The tumor formed a branching structure lying in the blood vessel. Many of these vessels still had their endothelial and elastic coats intact. In other instances where the above means did not suffice to show that the tumor was connected with the thrombus, serial sections demonstrated this. Pictures suggestive of transitions between liver cells and tumor cells were not encountered.

The tumor cells were not pigmented. They were smaller than the liver cells and their nuclei presented a more variable appearance. Mitoses were not infrequent. The cells were arranged in columns which were separated from each other by a delicate capillary stroma. In the center of the smaller vein nodules, the cells were larger and resembled more closely liver cells.

Case No. 3.—This case was reported by Miss Catherine H. Travis in *The Johns Hopkins Hospital Bulletin*, 1902, XIII, 108.

T. S., colored male, aged 40 years. Patient was admitted to the medical clinic of The Johns Hopkins Hospital February 5, 1901. From July, 1900, he had had attacks of nausea lasting for several days. At Christmas he was seized by a sharp pain in the region of the liver, which became a dull, constant ache. On examination, the liver was found much enlarged and presented several nodular protuberances along its border. On March 3 he was discharged unimproved. April 4 he was seen at his home and found to have a marked ascites. Paracentesis was performed, and four or five liters of fluid resembling pure blood were withdrawn from the peritoneal cavity.

Autopsy (No. 1710) performed 26 hours after death by Dr. MacCallum. *Anatomical Diagnosis:* Primary carcinoma of the liver; invasion of portal and hepatic veins; implantations in the peritoneum; metastases in pulmonary artery and lungs; ascites; hemoperitoneum.

Body is that of a rather emaciated negro man. The abdomen is distended slightly. The peritoneal cavity contains one and one-half liters of blood-stained fluid, and the dependent portions are filled with a postmortem blood clot. In the mesentery of the sigmoid flexure is a soft purplish thrombus like mass lying under the blood clot and quite adherent to the peritoneum. In the pelvis there is a similar but larger mass 5 x 3 x 2 cm. adherent to the peritoneum over the rectum. Numerous small, opaque yellowish nodules project under the pleura of both lungs, measuring from

2 to 10 mm. in diameter. On section these are yellowish, opaque, and are pasty in consistence. The main artery of the left lung contains strands and masses of soft yellowish, granular, very friable material, and on opening the vessel this is found to enter the branches of the vessel. On section the finer arterial branches are found to be here and there injected, as it were, with the opaque yellow material so as to show through the œdematous lung substance as branching, tree-like structures. Many of these may be traced to the nodules described beneath the pleura.

Liver measures 32 x 26 x 15 cm., and weighs 3580 grams. The presence of a few adhesions and a slightly thickened capsule makes the surface of the right lobe relatively smooth; elsewhere it is coarsely granular. The surface is mottled; dark green and yellow areas stud the grayish-pink ground substance. There are numerous yellowish elevated nodules, sometimes reaching the diameter of 4 cm., under the capsule, and several large globular masses, quite soft and fluctuant, project from under the surface. A similar large mass extends into the peritoneal cavity to the right of the gall bladder. The superficial portion of this forms a pasty necrotic mass to which a blood clot is adherent. On section the liver presents a variegated appearance; the greater part of the right lobe is occupied by a large, spherical tumor measuring 16 cm. in diameter. This mass is sharply defined from the surrounding liver tissue, particularly on its right side where a dense fibrous capsule has been formed. On the left side near the hilus it has invaded the portal vein and completely occludes it. The tumor mass is coarsely trabeculated, composed of discolored bands of fibrous tissue, in the meshes of which a friable pasty mass of varying color is found. As the median portion of this section is approached other large masses of tumor tissue occur which are in a better stage of preservation.

The periphery of the right lobe of the liver is markedly compressed, as above stated, but the liver tissue is still here definitely discernible. It is deeply bile stained. The lobules are irregular, in part greatly compressed, in part distorted by dense bands of fibrous tissue. In the left lobe there is no large tumor mass. On section the cut surface, as well as the outer surface, has a nodular appearance and seems to be made up of large, independent, rounded masses, held together by a firm framework of connective tissue. Some of these rounded areas are olive green, others a yellowish-fawn color, and others hemorrhagic and more opaque; they may often be easily shelled out of the trunks of large veins. The large thrombus in the portal vein fills all of the branches of the right lobe of the liver, but only projects for a short distance into some of the branches of the left lobe. The superior vena cava is likewise filled with a tumor mass which projects into it from the mouths of the hepatic veins.

The liver tissue is everywhere divided by irregular bands of fibrous tissue into smaller and larger false lobules. The cirrhotic process is easily made out, even in areas where no tumor tissue occurs. In the region of the tumor, however, the fibrous tissue is much more conspicuous. The liver tissue itself in many places has the appearance of adipose tissue, the liver cells have disappeared entirely and in their place vacuole like structures appearing as signet rings are found. Such areas may involve the whole or the periphery of a false lobule, encapsulated by fibrous tissue. The liver tissue in many places is entirely necrotic, and here and there is invaded by polymorphonuclear leucocytes. In other areas the dead tissue is diffused with blood.

The fibrous tissue septa are everywhere conspicuous. They form irregular bands in which the usual bile duct like structures and small round cells are found. Smaller and larger nests of liver tissue also occur. They are always well preserved, healthy young liver cells, arranged in columns, but not bearing any specific relation to vessels. These are characteristic hyperplastic nodules so frequently found in cirrhosis of the liver. Similar areas of hyperplasia of the liver cells are sometimes found at the periphery of lobules, for it is particularly the central zone which is involved in the necrotic process.

The tumor nodules are variable in size, show definite areas of necrosis, and are consequently not always distinct. All of the small nodules seem definitely encapsulated; they frequently show communications with larger masses which no doubt lie in the larger blood vessels and, in many places by their growth, compress the liver columns concentrically. The invasion of the strands of tumor cells into the interacinar capillaries brings about pictures closely resembling the so-called transitions described in the other two cases, but the distinction between the tumor cells and the liver cells may be readily made out. The tumor nodules are composed of strands or nests of cells having only a capillary stroma. The strands vary in size and branch frequently. All of these cords have an endothelial covering. The tumor cells are smaller than the liver cells and stain more deeply with hematoxylin. Mitotic figures occur rarely. The nuclei, however, differ in the intensity with which they absorb the hematoxylin. Some of them are small, deeply stained, while many of them are large and vesicular with several nucleoli. Here and there small gland-like formations occur. These appear as small lumina surrounded by tumor cells—the lumina vary in size and apparently are artifacts or cyst-like structures within the tumor. In many places the tumor cells are very necrotic. In the larger nodules the necrosis involves the entire tumor.

To summarize: Patient was a colored male, aged 40. The disease had only manifested itself about nine months before death. The cardinal features were abdominal pain, enlarged nodular liver, hemorrhagic ascites. At autopsy the liver was much enlarged and had an irregular surface. One tumor nodule formed a polyp-like mass on the surface and from the necrotic surface of this nodule hemorrhage had occurred into the peritoneal cavity. On section the tumor filled most of the right lobe and studded the left lobe with small nodules.

The portal vein and most of its intrahepatic branches, as well as the hepatic vein and vena cava, were filled with the tumor. This was also true of many of the branches of the pulmonary artery. Most of the smaller nodules in the liver were sharply circumscribed and it could be readily demonstrated that they were simply cords of the occluded veins. Microscopically there was a definite cirrhosis even in the areas uninvolved by the tumor process. In the cirrhotic areas regenerating islands of liver cells, bile ducts, and round cells, occur. In the region of the tumor nodule the fibrosis was much more marked. Here the liver cells showed atrophy and necrosis. The tumor cells were easily distinguishable from the cells of the hyperplastic liver nodules. They formed columns and nests separated from each other only by capillary stroma. In some instances the tumors invaded the intrahepatic capillaries and in this way brought about pictures suggestive of transitions between liver cells and tumor cells.

Case No. 4.—This case was reported in detail by Fabyan[24] in 1907 (*The Johns Hopkins Hospital Bulletin*, XVIII, 351), and therefore only a brief abstract will be given here.

The patient was a colored male, aged 62, who had been ill for a long time with weakness and abdominal distention. Physical examination showed him to be markedly emaciated. The liver was large, hard and nodular. At autopsy three quarts of straw colored fluid were found in the abdominal cavity. The vena cava contained a large tumor thrombus. The liver was small, measuring 21 x 14 x 7 cm. and weighed 1300 grams. The surface was nodular. These nodules varied from 0.5 to 3 cm. in diameter, and had a grayish-yellow color, contrasting with the purplish red liver tissue. A few nodules were bile stained. The portal vein and many of its intrahepatic branches were filled with thrombus. On section most of the right lobe of the liver was replaced by small nodules of new growth. These were also present throughout the rest of the organ, but were not so numerous. The largest nodules were about 3 cm. in diameter. Many of them were distinctly encapsulated.

Microscopically the liver showed a cirrhosis of the annular type, with nodular areas of hyperplastic liver cells. In many places the liver cells showed pressure atrophy and congestion atrophy and other evidences of disintegration. The liver cells were in part replaced by connective tissue. The tumor nodules were usually circumscribed by more or less connective tissue, but here and there they were continuous with the liver cells. The tumor cells were grouped together in masses or in coarse trabeculæ, which were only separated by delicate capillary stroma. They varied in size and in staining intensity. Their nuclei, usually larger than liver nuclei, were vesicular, but nuclear figures and multinucleated cells were abundant. Many of the portal vessels were plugged by masses of tumor cells and still showed their endothelial lining. The lungs contained tumor nodules, and microscopically the blood vessels of the lungs were plugged with tumor masses, just as in the portal vein and vena cava.

The following two cases lack histories and protocols, and the notes were made entirely from Kaiserling specimens.

Museum No. 2154. The specimen consists of a tranverse section through the hilus of the liver. The liver tissue is readily distinguished from the tumor tissue—the former has a grayish-green color, while the latter is grayish-yellow. The liver tissue is much distorted due to the presence of the tumor masses, and in the section no large area of liver tissue uninvolved by tumor is found. The tumor tissue is divided into larger and smaller lobules which occupy the greater portion of the specimen. In a few places these are discolored, apparently bile stained. The portal vein and most of its intra-hepatic branches, as far as can be made out, are plugged by tumor masses which on section have a stringy appearance. On the very edge of the liver where the tumor is not so conspicuous, definitely circumscribed, small, round nodules of tumor tissue are found which probably are sections of intra-vascular tumor thrombi.

Microscopically, in those areas, uninvolved by the tumor, no marked increase in fibrous tissue is to be found. Here and there the connective tissue about the periportal space is thickened, and in it there are some round cells. In the region of the tumor the liver cells are compressed and atrophic, and here the fibrous tissue is much more conspicuous. In these areas an occasional nodule of hyperplastic liver cells may be seen. In other areas the liver cells are undergoing disintegration and show fatty change. The tumor nodules vary somewhat in appearance, the smaller ones are definitely circumscribed, and the connective tissue surrounding them has an inner, endothelial lining. Some of these nodules give off bud-like branches which project into the surrounding interacinar liver tissue. Such nodules are always found in the thickened, periportal connective tissue. These small nodules are well preserved, and are composed of polyhedral cells arranged in columns and clumps, and separated from each other by a capillary stroma. In the larger ones the central areas are not so well preserved and appear as small necrotic areas. Larger tumor masses are found where the relation of the blood vessel is not distinct. These larger nodules, however, cause a concentric flattening of the surrounding liver cells. They are composed of numerous islands of tumor tissue similar to that described in the smaller venules. Each island seems to have an endothelial sheath, but between these sheaths no fibrous tissue is to be found. In the center of the islands, necrosis often occurs, and many of the tumor cells show mitoses. In other areas the tumor cells tend to form tubular or rosette-like structures, but even here no connective tissue stroma is to be found. The tumor cells vary considerably in their appearance. In some of the larger nodules their protoplasm stains pinkish with eosin and the nuclei are much more pyknotic, while in all of the smaller nodules and particularly in the well preserved masses lying within the blood vessels they have the appearance above described. That is, they are polyhedral in shape, stain pale blue with hæmatoxylin are coarsely granular, have vesicular nuclei and show frequent mitoses.

To summarize: The portions of the liver uninvolved by tumor show only a very slight cirrhosis. The tumor nodules bring about atrophy and necrosis of the liver cells, which is followed by fibrosis. All of the smaller tumor nodules are definitely within the blood vessels, while the larger ones have invaded the vessel wall, and brought about a concentric flattening of the surrounding liver cells. The tumor cells form columns of many rows or solid nests of cells, always separated from each other by a capillary stroma. In some places duct-like and gland-like structures are produced, but these contain no connective tissue between them, and the clefts are never long. The tumor cells are readily distinguished from the liver cells in most instances, but in the older nodules, where the tumor cells are not well preserved, they resemble more closely the liver cells.

Museum No. 1207. The specimen consists of two definite kinds of tissue. The liver tissue which forms one portion of the specimen is coarsely granular on its surface, and on section strands of fibrous tissue course through it, forming larger and smaller lobules. The normal architecture is here absolutely obliterated. The other tissue is more spongy in character, and occurs as definitely circumscribed nodules throughout the greater part of the section. In some places these seem to fuse and form larger tumor masses.

Microscopically, throughout the section, even in those areas where no tumor nodules are to be made out, the periportal connective tissue is considerably increased. It forms large areas in which bile duct like structures and many round cells are found. An occasional small area of hyperplastic liver cells occurs, and in some places bile duct like structures, lying in the fibrous tissue at the periphery of the tumor nodule, are so numerous that they produce an adenoma like picture. The tumor nodules compress the liver cells whenever they attain any size, while smaller nodules seem to be enclosed in blood vessels. The tumor cells are arranged in a regular trabecular order; often four or five cells abreast, and sometimes forming solid clumps. In the larger blood vessels this produces a villous like appearance. Each cord is surrounded by an endothelial sheath and between the cords blood is found. The cells are not very well preserved. They are, as nearly as can be made out polyhedral in shape, coarsely granular, pale blue staining with large vesicular nuclei—the nuclei vary in chromatin content and some multinucleated cells are found.

To summarize: The liver is markedly cirrhotic throughout. In the region of the tumors, the fibrous tissue proliferation is more conspicuous and is associated with atrophy of the liver cells. The tumor nodules are composed of columns of polyhedral cells, and these columns are only separated from each other by a capillary stroma. The smaller nodules are confined to the blood vessels, but in the specimen the origin of the larger nodules could not be demonstrated.

It will be of interest now to compare the results of the study of the six preceding cases with the current conception regarding primary carcinoma of the liver.

Occurrence.—The first three of these cases are the only positive instances of primary carcinoma of the liver occurring in 3700 post-mortem examinations at The Johns Hopkins Hospital. (There were two other possible instances of primary carcinoma of the liver, autopsies Nos. 33 and 45. In both of these the protocols were insufficient and since there was no tissue available for examination they could not be included.) This would give a percentage of 0.08 per cent somewhat higher than that of Hansemann and Rindfleisch, but much lower than that of Goldzieher and v. Bokay.

Age and Sex.—In the four instances where this was stated, the disease occurred in males between the fourth and sixth decades.

Clinically there was nothing characteristic of the specific condition. The symptoms and signs were similar to those occurring in cirrhosis of the liver. Added to this the rapid course of the disease, the presence of hemorrhagic ascites and an enlarged, irregularly nodular liver indicated the malignant nature of the condition.

Histogenesis.—In all of the above cases the tumor originated from the liver cells themselves. The cells of the tumor resembled the liver cells. They were somewhat smaller, and had a less regularly granular protoplasm with a much greater affinity for hematoxylin than the protoplasm of the liver cells. With hematoxylin and eosin the protoplasm of the tumor cells stained pale blue, while that of the liver cells stained pink. The nuclei were, as a rule, larger and more vesicular than those of the liver cells, but the size of the nuclei and their chromatin content varied considerably, and small pyknotic ones were not infrequent. Mitotic figures were always demonstrable in the tumor nodules, and cells with several nuclei were found here and there.

The tumors had a trabecular structure and were composed of columns of cells similar to those of the normal liver acini though, as a rule, these columns were much thicker and often had ten or more cells abreast. In some instances these were so thick that solid nests of cells were formed. Between the columns or surrounding the solid nests was a layer of endothelial cells. These were part of the capillary stroma which occurred throughout the tumor. No definite connective tissue stroma was to be found in any of the cases.

In some instances the tumor had a more glandular structure. All transitions occurred from simple, crevice-like dilatations between the cells of the columns to lumina similar to those of the bile ducts and rosette-like nodules. The latter were composed of a variable number of rows of tumor cells, arranged with their long axis perpendicular to a central lumen, as in a perithelioma. The various cavities in the tumor nodules, when cut longitudinally, were short, and the cells surrounding many of them were compressed. Their possible production by a simple dilatation of pre-existing intercellular spaces or bile capillaries, as suggested by Yamagiwa, *et al.*, seems plausible. The more definite structures like the rosettes which occurred particularly in the tumor thrombi, are probably the result of a reversion of the tumor to the embryonic structure of the liver. These glandular and tubular structures were not sufficiently conspicuous in any case to confuse the picture.

Necrosis occurred particularly in the larger tumor thrombi and in many smaller tumor nodules. In many of these there were multiple centers of necrosis and in this way false glandular structures were produced. Cells in process of disintegration often resembled the normal liver cells closely. Their protoplasm stained pale pink and their nuclei were smaller and more deeply staining.

Relation to Cirrhosis.—In all of the cases there was a marked cirrhosis in association with multiple tumor nodules. In two, however, relatively large areas of liver, uninvolved by tumor nodules, were entirely free of the cirrhotic process. On further examination the following facts, which, of course, are well known but which are not usually emphasized, became evident. The liver suffers greatly from the presence of the tumor. The tumor nodules compress the surrounding liver tissue which may be seen as concentric layers of more or less atrophied columns of liver cells. In many places the liver cells have entirely disappeared and in their place there is a condensation and a fibrosis of the pre-existing stroma. This appears as dense bands of fibrous tissue surrounding the larger tumor nodules more or less completely. In other areas the plugging of the vascular trunks results in a tremendous dilatation of the intra-acinar capillaries. This is associated with an atrophy of the liver cells and in some areas these processes are so extensive that a picture similar to an angioma is produced. In still other areas definite necrosis of the hepatic parenchyma occurs, probably brought about by the extensive tumor thrombi.

In these three ways at least fibrosis may result from the effect of the cancer upon the hepatic parenchyma, and bring about a cirrhosis secondary to the tumor growth. An analogous process was described by Ziegler in his text-book, but Eggel was unable to find any similar cases in his exhaustive review of the literature in 1901, and since his time the possibility of a picture simulating a true cirrhosis, but secondary to the tumor growth, has not been emphasized.

In some instances, also, so much of the liver is involved by the tumor that it is difficult to obtain areas of any sufficient size uninvolved by tumor to study the cirrhotic process, and in these it may be impossible to determine the relation between the two conditions. In the other four cases the cirrhosis was marked even in those areas uninvolved by tumor. It is, therefore, evident that the cirrhosis is not, in all cases, entirely dependent upon the new growth and the general consensus of opinion, that the cirrhosis precedes the neoplasm, is probably correct. Whether a picture of cirrhosis may be produced secondary to the tumor growth cannot be said with certainty from the preceding two cases. That the cirrhotic process is greatly exaggerated, both macroscopically and microscopically, as a result of the innumerable tumor nodules scattered through the hepatic parenchyma, is evident.

The secondary occurrence of neoplasms as a result of chronic inflammatory process is of the boardest interest. It has been emphasized recently by Verse,[25] Winternitz and Boggs,[26] etc., and it is unnecessary to enter into the discussion of the problem here. It will suffice to say that the frequency of the occurrence of cancer, secondary to cirrhosis of the liver, is important confirmation of the theory. As a result of the destruction of the liver cells there is repair which manifests itself, on the one hand, by a proliferation of the interstitial tissue producing a cirrhosis, and on the other hand, by an hypertrophy and hyperplasia of the liver cells which produce the hyperplastic liver nodules similar to adenomata so frequently found in cirrhotic livers. As the irritating or destroying process continues, the cirrhosis becomes more marked, and the liver cells, called upon more and more to compensate for those that have been destroyed, may gradually lose their more specific functions and only retain their vegetative capacity. In this way a malignant neoplasm may arise.

Mode of Growth.—In order to understand the nature of the transition pictures between liver and tumor cells at the periphery of the tumor nodules, and the apparent multicentric origin of the neoplasm, the grosser details of the tumor growth will be considered first.

In all of the six cases many of the blood vessels contained tumor thrombi. In several where the entire liver could be studied these tumor thrombi were by far the most conspicuous part of the growth. They formed long strands and streamers which could be followed through, and dissected from, the portal vessels. Nodular enlargements were also found along their course and they even occurred at the very periphery, just under the capsule of the liver. Naturally the conclusion was reached that the tumor started in one area, invaded the portal system, and in this way involved more or less of the liver secondarily. This was the more interesting since a preceding report of one of these cases from this laboratory had confirmed the conception that the tumor was multicentric in origin, and that transitions between liver cells and tumor cells were demonstrable at the periphery of the nodules.

These cases were, therefore, carefully investigated. In Cases 1 and 2 the extensive macroscopic tumor thrombi were confirmed and emphasized by the microscopic picture. The great majority of the tumor nodules were contained within the portal veins. The vessel wall in most instances still had an intact endothelial lining, the elastica could be readily stained and where these were not sufficient, serial sections showed the connection between the tumor nodule and the thrombus. Such a thrombus cut longitudinally showed a most characteristic picture. Its branches corresponded with the vascular bed and these varying sized ramifications invaded the liver tissue everywhere as larger and smaller strands, sheathed by a vessel wall, in a more or less perfect stage of preservation. In Case 3 the large portal vein at the hilus of the liver was invaded by the large tumor in the right lobe of the liver, but as was seen in the gross examination the thrombus did not invade all of the branches of the vein supplying the left lobe. Microscopically, also, many of the portal branches were free of tumor cords, but on the other hand many of the tumor nodules were surrounded by endothelium, as emphasized by Miss Travis in her report of this case. Throughout, pictures similar to those described in Cases 1 and 2 were found, and this was true also of the other three cases.

Pictures suggestive of transitions between liver cells and tumor cells at the periphery of the smaller nodules occurred, but these were rare, and they did not form a distinct group; various relations between the tumor nodules and the hepatic parenchyma were found. Some nodules as we have seen were definitely enclosed within a thick walled vein, others invaded the vein wall or grew out through a thinner walled vessel into the hepatic parenchyma. In many of these remnants of the thinned vessel wall remained only in one area. Around these nodules the columns of liver cells were frequently flattened and compressed as above described, while in others, cords of tumor cells ran out into the intra-acinar capillaries or through the vein wall into the liver columns themselves. In these latter instances pictures resembling transitions between liver cell and tumor cell occurred. These, however, were rare, and, in view of the numerous intermediary stages and the vascular invasion, it seemed hardly necessary to assume that these were actually transitions.

The presence, therefore, of a larger nodule in the right lobe of the liver (and this was particularly true of Case No. 3) and the extensive plugging of the portal radicals with tumor thrombi, led to the conclusion that the tumor was unicentric in origin in all these cases, and that the multiple nodules were, in part sections of tumor cords which filled the portal vein, in part, the result of emboli from the same source. Fabyan had reached the same conclusion in regard to Case 4, as may be gathered from the following sentence: "The invasion of the lymphatics and blood vessels seems to be an important characteristic of this type of tumor, and though no actual invasion was noted under the microscope in this case, it has been seen in other instances. Given an invasion of the portal system with new growth, the diffuse distribution throughout the liver is easily accounted for."

While it is impossible to draw any sweeping conclusion concerning the unicentric origin of primary cancer of the liver from so few cases, there are certain well-known facts which strengthen this conception. The very definition of the cancer arising from the liver cells is dependent upon the fact that it invades the blood vessels, and only in this way does it differ in many instances from the benign adenoma. This was emphasized by all of the older writers and v. Heukelom particularly pointed it out, mentioning its occurrence in more than three-quarters of the cases reported. In his own cases he could not exclude the possibility that the tumor had invaded the liver through the portal veins, but this he considered improbable on account of the pictures of transition. In Eggel's series, too, venous tumor thrombi were a most frequent occurrence, and it is not unlikely that it occurs in every case where multiple tumor nodules are found in the liver.

With the tumor thrombi occurring constantly it would seem that nothing further were necessary to explain the multiple nodules and that they were simply metastases. v. Heukelom could not accept this view on account of the frequent transitions between liver cells and tumor cells at the periphery of the smaller nodules. These transitions now, however, have become far less important and as we have seen are not accepted by many, and considered as rare occurrences by others. It seems, therefore, that it may be said with reasonable assurance that primary cancer of the liver is unicentric in origin, as a rule at least, and that in most instances, if not always, the so-called transitions are artifacts. Yamagiwa's standpoint that since the hyperplastic liver nodules occur in many neighboring areas, *i. e.*, are multicentric, therefore cancer should be multicentric in origin, may be theoretically correct, but there seems no basis for the assumption that if one hyperplastic nodule assumes cancerous manifestations this should occur in many such nodules.

The theory that these tumors increased in size by a constant metaplasia of liver cells to tumor cells has been less and less advocated as the so-called transitions became rarer and better understood. In the above cases there was no evidence to support this appositional growth; instead the presence of numerous mitoses, as is usually found in malignant tumors, seemed to indicate that the growth of the neoplasm was entirely autogenous.

Extra-hepatic Metastases.—Even though metastases occurred in the lungs in the four cases of the above series where there were complete protocols, the metastatic nodules were very small. This is not what might have been expected with the extensive vascular involvement that was present. In several instances, the tumor grew up the cava and into the pulmonary artery, still there were only a few nodules in the lung tissue. The absence of extensive extra-hepatic metastases in cancer of the liver has been repeatedly emphasized. This is, of course, not unique for this tumor, but the question why certain tumors metastasize generally, while others, like cancer of the prostate, have a predilection for bone, etc., is of the broadest interest. It is not only true of neoplasms but occurs likewise with various infectious processes.*

The recent work of Levin,[27] on the mechanism of the organ resistance to experimentally inoculated cancer into the testicle of white rats, deals directly with this problem. In this specific instance Levin found that, while the normal testicle was resistant to implanted cancer, it was possible to render the same testicle artificially susceptible to the growth of the tumor by killing off some of the tubular epithelium with *Scharlach R* oil or 4 per cent ether water. Levin concludes that the "growth of cancer, then, presents a loss of equilibrium between the inhibitory power of the parenchymatous cells and the proliferating power of the cancer cells."

SUMMARY AND CONCLUSIONS.

Primary carcinoma of the liver is a rare condition occurring in from .028 per cent to 0.3 per cent of all autopsies, according to various statistics.

It occurs most frequently in adult males but is proportionately relatively common in females and may occur at any age. A number of cases have been described in infancy.

Clinically the disease is difficult to differentiate from cirrhosis of the liver. Its rapid course, the presence of an enlarged irregularly nodular liver, hemorrhagic ascites, or metastases in accessible regions, which is exceedingly rare, may be of assistance in the diagnosis.

The tumor may occur in normal or in diseased livers. In a tremendous percentage of cases the liver presents an ordinary type of cirrhosis, but various other types of chronic hepatitis caused by syphilis, parasites, etc., may occur. The tumor itself may be only one large nodule. This may have smaller ones at its periphery, and in this way transitions occur until the entire organ is studded with varying sized nodules. Any division between these forms is simply arbitrary and subserves no useful purpose.

The tumor may arise either from the smaller bile ducts or from the liver cells. The names "carcinoma cholangiocellulare" and "carcinoma hepaticellulare" may be used to differentiate them as suggested by Goldzieher and v. Bokay. The liver cell tumor may be bile stained, but this does not differentiate it absolutely from the duct cancer, for bile pigment may be found in the lumina of the nodules of the latter. The liver cell cancer has a trabecular structure. It is composed of thick columns of cells not very unlike normal liver cells which may be arranged in solid nests and show here and there a glandular structure. Its stroma is always composed of a simple capillary net similar to the interstitial tissue of the liver acinus. The bile duct cancers have a tubulo-adenomatous structure and a more or less dense connective tissue stroma.

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* This has been discussed in a recent article upon Primary Tuberculosis of the Spleen. Arch. of Int. Med., 1912, V. X, by the author.

It is generally agreed that the cirrhosis precedes the neoplastic formation where these two are associated. The tumor, however, brings about pressure atrophy directly and necrosis of the hepatic parenchyma through its extensive vascular involvement, and in this way a fibrosis may result secondary to the tumor growth. This is important, since in a few cases those areas of liver uninvolved by tumor growth are likewise free of cirrhosis. Whether a cirrhosis may develop secondary to the tumor growth is uncertain, but there is no doubt that the cirrhotic process is exaggerated greatly as a result of this.

The secondary formation of cancer as a result of a chronic destructive process in the liver parenchyma finds its analogue in many malignant tumors elsewhere in the body. It may be interpreted in the following way: As a result of the destruction there is a constant demand for repair. The cells proliferate and lose their more specific functions until finally the equilibrium between function and growth is lost and certain cells become vegetative. The constant occurrence of the reparative phenomena is manifested in the liver by the hyperplastic liver nodules so frequently found in cirrhosis, and these are supposed by many to be the source of the liver cell cancers.

Primary cancers of the liver are differentiated from benign adenomata chiefly by their power to invade the blood vessels. The portal vein is most frequently invaded and all of its radicals may be plugged with tumor thrombi. In some instances, practically no tumor remains after the growth in the blood vessels is removed. But in any case, given an invasion of the portal system, the diffuse distribution in the liver is easily accounted for. The so-called transition from liver cells to tumor cells at the periphery of the tumor nodules is denied by many and considered to be extremely rare by most of the rest of the writers since v. Heukelom. In most instances it is probably an artifact brought about by an invasion of the liver acini by the tumor thrombi or emboli. Granted this, there is no longer any basis either for the theory of multicentric origin of cancer of the liver or that its subsequent development is brought about by an appositional growth.

The tumor is not in any respect unique. It is unicentric in origin, distributes itself through the vascular system, forming a more or less diffuse growth in the liver, and develops autogenously. The rarity of extensive extra-hepatic metastases in view of the tremendous tumor thrombi, which not only involve the portal but also the hepatic veins and the vena cava, is worthy of note.

LITERATURE.

1. v. HANSEMANN: Ueber den primären Krebs der Leber. Berl. klin. Wchnschr., 1890, XXVII, 353.
2. GOLDZIEHER UND V. BOKAY: Der primäre Leber Krebs. Virchow's Arch., 1911, CCIII, 75.
3. YAMAGIWA: Zur Kenntniss des primären parenchymatosen Leberkarcinom (Hepatoma). Virchow's Arch., 1911, CCVI, 437.
4. HANOT ET GILBERT: Étude sur les maladies du foie. Paris, 1888.
5. KARSNER: A Clinico-Pathological Study of Primary Carcinoma of the Liver. Arch. Int. M., 1911, VIII, 238.
6. KELSCH ET KIENER: Contribution à l'étude de l'adenome du foie. Arch. de Physiol., 1876, 2. s. III, 622.
7. SABOURIN: Contribution à l'étude des lésions du parenchyme hepatique dans la cirrhose. Essai sur l'adénome du foie. Thesis, Paris, 1881.
8. v. HEUKELOM: Das Adenokarzinom der Leber mit Cirrhose. Ziegler's Beitr., 1894, XVI, 241.
9. MARCKWALD: Das multiple Adenom der Leber. Virchow's Arch., 1896, CXLIV, 29.
10. FROHMAN: Ueber das Leber Adenom, etc. Inaugural Dissertation, Konigsberg, 1894.
11. RIBBERT: Das Karzinom, Bonn, 1911. Das Maligne Adenom der Leber. Deutsche med. Wchnschr., 1909, XXXV, 1607; Lehrbuch der pathologischen Histologie, 1898.
12. WEGELIN: Ueber das Adenokarcinom und Adenom der Leber. Virchow's Arch., 1905, CLXXIX, 95.
13. ZIEGLER: Lehrbuch der allgemeinen und speciellen pathologischen Anatomie, 1902, II.

14. Eggel: Ueber das primäre Karzinom der Leber. Ziegler's Beitr., 1901, XXX, 506.
15. Herxheimer: Ueber einen Fall von Adenokarzinom der Leber. Centralbl. f. allg. Path. u. path. Anat., 1902, XXXIV, 705.
16. Loehlein: Drei Falle von primären Leberkarcinoms. Ziegler's Beitr., 1907, XLII, 531.
17. Fischer: Ueber Gallengangs-Karzinom sowie über Adenom und primäre Krebse der Leberzellen. Virchow's Arch., 1903, CLXXIV, 544.
18. Dibbelt: Ueber Hyperplasie, Adenom und Primärkrebs der Leber. Inaugural Dissertation, Greifswald, 1903.
19. Schmieden: Lebercirrhose und multiple Adenombildung. Virchow's Arch., 1900, CLIX, 290.
20. Theodorow: Zur Kenntniss der primären Lebercarcinom. Virchow's Arch., 1908, CXCIII, 407.
21. v. Schuppel: Ziemsen's Handbuch, 1878, VIII, 284.
22. Heussi: Ueber das Wachsthum des Adenocarcinoms der Leber. Inaugural Dissertation, Zurich, 1898.
23. Travis: A Case of Multiple Primary Adenocarcinomata of the Liver with Cirrhosis. Johns Hopkins Hosp. Bull., 1902, XIII, 108.
24. Fabyan: A Case of Primary Carcinoma Supervening in a Cirrhotic Liver. Johns Hopkins Hosp. Bull., 1907, XVIII, 351.
25. Verse: Arbeiten aus dem pathologischen Institut zu Leipzig, 1898.
26. Winternitz and Boggs: A Unique Coincidence of Multiple Subcutaneous Hæmangio-Endothelioma, etc. Johns Hopkins Hosp. Bull., 1910, XXI, 203.
27. Levin: Studies on Immunity on Cancers of the White Rats. J. Exp. M., 1912, XV, 163.

THE STATISTICAL EXPERIENCE DATA OF THE JOHNS HOPKINS HOSPITAL, BALTIMORE, MD., 1892-1911.

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Introduction.—In few departments of statistical research is there more urgent need of improvement and reform than in the vast and almost unexplored domain of hospital experience. For reasons which cannot be discussed on this occasion, the statistical data of American hospitals have been a subject of almost universal indifference and, with few exceptions, the published data are of small, if any, practical utility. According to a table published in the Journal of the American Medical Association of Nov. 9, 1912, there were in 1911, 4,292 hospitals and sanatoria in the United States, with a bed accommodation of 260,643. In the census report for 1904, only 822 hospitals were enumerated, but the wide disparity in numbers is probably the result of differences in classification, since, evidently, the term "hospital" is one which does not admit of precise definition. It is of interest, however, to note that the number of patients in the hospitals referred to on Jan. 1, 1904, was 71,427 and that the number of patients admitted during the year was 1,064,512, leaving the number remaining on Dec. 31, 1904, as 71,530.*

Importance of Hospital Statistics.—The census report contains no information of a medical character and no distinction is made as regards the class of patients admitted, or the method of treatment and results. It would, however, seem to require no argument to sustain the conclusion that accurate and trustworthy information concerning so important a subject as institutional treatment for disease or injury should be available in a concise and practically useful form. As a matter of fact, that is not the case for any state, or even city, of the United States at the present time, and, with few exceptions, the hospital returns, as published, are therefore of very limited practical value. At the same time, it may be said that the necessary scientific classification, tabulation and periodical publication of hospital statistics is neither a very difficult nor an expensive task, provided the work is done with the degree of medical and statistical skill essential to an investigation of this kind.

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* According to an editorial in "The Modern Hospital," Sept., 1913,

"There are in the United States 6,665 institutions of record for the care of the sick, with a total capacity of more than 600,000 beds. By a modest estimate, these huge figures represent a money investment in land, buildings, and equipment of not less than $1,500,000,000, and an annual outlay for maintenance approaching $250,000,000.

"On the human side, there are more than 100,000 trustees of hospitals, and more than 65,000 physicians on hospital medical staffs. About 10,000,000 men and women contribute annually to hospital funds, and approximately 9,000,000 men, women, and children are patients in the hospitals in the course of each year."

Extent of Hospital Accommodation.—It has properly been pointed out by M. E. McCalmont, R. N., in a suggestion for a Bureau of Hospital Information, that there are few commercial enterprises with such an enormous investment of capital as hospitals and allied institutions in the United States. According to this writer, in an article in the Dietetic and Hygienic Gazette, the estimated investment represents $537,000,000, and an annual expenditure of $107,000,000 for maintenance, enlargement and improvements. As a step towards increased efficiency and the protection of the public health, a resolution was adopted by the American Hospital Association, at its thirteenth convention, favoring a bill to be enacted by Congress, providing for the establishment of a Division in the United States Public Health Service, with power to collect and receive, and to classify and maintain, in such manner as may be made accessible, all important information relating to hospitals throughout the United States, but without specific reference to the urgent need of a qualified statistical analysis of the medical and surgical experience data, which may safely be asserted to be of vastly more public importance than the facts of financial administration. Recalling, in this connection, an address on "The Relation of the Hospital to Medical Education and Research," by Dr. Wm. H. Welch, and published in the Journal of the American Medical Association, under date of Aug. 17, 1907, it may be pointed out that the truly enormous experience of American hospitals has not been made use of to anything like the possible and desirable extent that the public importance of the data demand.

Practical Utility of Hospital Statistics.—The subject of hospital statistics and their practical utility has been before the public for many years. Certainly as early as 1852, an important discussion was published on the Vital Statistics of the Royal Free Hospital, in a contribution to the London Journal of Medicine. In 1861 Dr. John Charles Steele, Superintendent of Guy's Hospital, London, read an admirable paper on "The Numerical Analysis of the Patients Treated in the Hospital for the Last Seven Years, 1854-1860," before the Royal Statistical Society, including a discussion of the essential facts concerning 32,813 patients, of whom 2,978, or 9.1 per cent, had died. The tabular analysis makes the proper and absolutely essential distinction of medical and surgical cases, with a due consideration of the elements of age and sex, the classes of diseases treated, and the results. According to this analysis, the fatality rate during the years 1854-1860 was 14 per cent for medical cases, against only 5.6 per cent for surgical cases; but a further inquiry disclosed the fact that in medical cases the fatality rate had been 15.8 per cent for males against 11.8 per cent for females, while in surgical cases the mortality rate had been 6 per cent for male patients and 4.2 per cent for female patients. The analysis, therefore, even at this early priod, conclusively established the fallacy inherent in nearly all modern hospital statistics, of combining the sexes in the published returns, and quite frequently, also, the medical and surgical cases. In brief, the whole problem of hospital statistics was precisely presented in Guy's Hospital experience, 1854-1860, according to which the average fatility rate for all patients, whether medical or surgical, had been 9.1 per cent. The fatality rate had been as high as 15.8 per cent for male medical cases and as low as 4.2 per cent for female surgical cases. Since these differences are disclosed by every qualified analysis of hospital experience, it is obvious that all hospital statistics which combine male and female patients, or medical and surgical cases, are more or less seriously misleading. It requires to be pointed out also that the disparity in the fatality rate becomes much more pronounced when the various diseases or surgical operations are separately considered, with a due regard to the sex, age, race, etc., of the several classes of patients. At the present time, with the notable exception of The Johns Hopkins Hospital, there are very few, if any, hospitals in the United States for which the required information is available, to show precisely the results of hospital treatment, and even for The Johns Hopkins Hospital the information is not available in the published reports as regards the ages of patients, with reference to sex, color, diseases on admission, etc.

Need of Uniformity.—The paper by Dr. Steele was probably suggested by Florence Nightingale in a proposal made to the Fourth International Statistical Congress, held in London in 1860. The proposal, which was accepted by the Congress, included in a precise form a plan for uniform hospital statistics, amplified by a nomenclature of diseases, prepared by Dr. Farr. The following extract from the discussion upon the plan is of historical, as well as practical, interest:

> In the proposition made for a uniform scheme of hospital statistics by Miss Nightingale, that lady points out the defective state in which the general condition of hospital statistics is at the present time, the absence of any common nomenclature or classification of disease, the want of uniformity in the manner of tabulating facts, and, as a consequence, the comparative inutility of the vast mass of facts which have been accumulating in the hospital books of every country where such establishments exist. To remedy this defect in the future, she proposes the adoption in all hospital records of the nomenclature of diseases agreed to at preceding meetings of the International Statistical Congress; and as a nomenclature without some classification would involve the use of tables of unmanageable dimensions, she proposes that the classification which is now familiarly known in this country through the Registrar-General's Reports, and which has also been adopted in America, should be used in hospitals for practical purposes—an arrangement by which the dimensions of the forms she recommends have been reduced one-half. These forms, before being printed for use, were tried in several large hospitals; and a number of interesting results, obtained by them in connection with the comparative frequency and mortality of diseases at different ages and in different sexes, are given by Miss Nightingale. Several improvements also suggested themselves in the course of this experience, the results of which were embodied in those tables, which were laid before the Section, and have been adopted by it.

Elements of Hospital Statistics.—On April 16, 1867, Dr. Wm. A. Guy read a paper before the Royal Statistical Society on "The Mortality of London Hospitals," which remains to this day the classical illustration of statistical analysis of hospital experience data, with a due regard to all the essential factors more or less determining the rate of recovery and mortality in hospital experience throughout the world. The facts discussed by Dr. Guy were for the thirteen principal hospitals of the metropolis and for the period 1861-1865. The fatality rate for the combined experience was 9.7 per cent, but for medical cases the rate was 14.5 per cent and for surgical cases 6.5 per cent. The fatality rate was highest for male medical cases, or 17.4 per cent, and lowest for female surgical cases, or 6.1 per cent. Considering only patients in "special wards," representing probably what are now known as "private patients," the fatality rate among this class was only 1.5 per cent. The analysis included also a study of the mean length of stay, or duration of institutional treatment, which was found to be twenty-eight days for medical cases, thirty-two days for surgical cases, and thirty days for all cases.

A full discussion of this admirable paper is out of the question on this occasion, but it has seemed to me a fitting introduction to the present-day problem in the United States, of how the status of hospital statistics may be materially improved by an intelligent consideration of the essential facts which require to be taken into account.

General Morbidity by Race and Sex.—In American morbidity experience data, the elements of race and nativity require to be taken into account, in addition to the factors of sex, age, condition on admission, and mode of treatment. Particularly is this true for all our southern cities, where the negro population may be anywhere from one-tenth to two-thirds of the total population. For northern cities the race factor is frequently of less importance than the nativity of the patients, and in such cases at least a broad division should be made between the native and the foreign-born, with a possible subdivision for the leading nativities, typical of the community. It is most fortunate that in the published statistics of The Johns Hopkins Hospital the division by race has been maintained throughout, for without this distinction the statistical results would be of small value.

Plan and Scope of Nosography.—Aside from the required classification according to sex, age, race, and condition on admission, and whether medical or surgical, the proper nomenclature of diseases on admission is of considerable practical importance. Numerous attempts have been made for many years to provide a thoroughly satisfactory nomenclature of diseases, but none of the plans or systems of modern nosology can be considered entirely successful. The terminology, itself, is rather confusing, for while the term "nosography" stands for "a descriptive treatise on the character and nature of diseases," the term "nosology" stands for "the scientific classification of diseases," which, apparently, is the equivalent of "nosonomy," which, according to Gould, means "the nomenclature of diseases." "Nosonomy" also means "the study or science of the laws of disease," whereas "nosotaxy" is another term, according to Gould, for "the classification of diseases." The term "nosology" was adopted in the treatise by William Cullen, published in Philadelphia in 1816,* and, being derived from the early Latin, this term would seem to be best descriptive of the systematic arrangement of diseases into classes, orders, genera and species, amplified by accurate definitions and required explanations.

Bellevue Classification of Diseases.—It would carry me too far to discuss in detail the problem of disease nomenclature and classification. The classical discourse on the subject is an address by Dr. John W. S. Gouley, delivered before the New York State Medical Association on Sept. 28, 1887. Dr. Gouley favored the anatomical basis for a scientific classification of diseases. He defined the scope of nosography as including, first, the description; second, the definition; third, the nomenclature; and fourth, the classification, of diseases. To the nomenclature of diseases he gives the term "nosonomy," and to the classification of diseases the term "nosotaxy." It would be of value to have these terms better defined than is at present the case. As regards nomenclature and classification, I have accepted the Bellevue Hospital method, published in 1903, as most likely to be in conformity with present-day medical and surgical opinion. The classification can also be coördinated with the international classification of causes of death, as adopted by the census office, and by practically all boards of health throughout the country. Since this nomenclature and classification are in permanent use by one of the largest hospitals in the country,† it would seem best that other hospitals should conform, as near as practicable, to the Bellevue classification, so as to make the returns for the different institutions comparable. In any event, the Bellevue classification is a material improvement over the classification used in The Johns Hopkins Hospital statistics, and important technical difficulties in statistical treatment will be successfully overcome by its complete adoption by the hospitals of the United States and Canada.

The Problem of Morbidity.—The problem of general morbidity (as differentiated from institutional morbidity), considered from a medical as well as from an economic point of view, presents more serious scientific difficulties than the problem of mortality. The term "sickness" seems to defy precise definition, but what is called sickness occurs more or less throughout life and the ultimate cause of death may not have a definite relation to any of the various illnesses that have preceded it. In a general way, it may be said that the rate of sickness increases with age in adult life, and while there is about one week's sickness per annum at ages 20 to 25, there is about four weeks' sickness a year at ages 55 to 59. The term "sickness," as here used, includes accidents. According to German experience, the proportion of cases of sickness among wage-earners is about 37.3 per cent per annum, and the average number of days of sickness is 20.1 per case.* Considered from this point of view, sickness is evidently an economic problem of great practical importance, and a reduction in the rate of sickness is at least of equal significance to a reduction in the death rate. It has been estimated that to every death there is about two years' sickness, but this is partly conjectural. There are no facts which warrant a precise conclusion as to what the average amount of sickness in the United States is at the present time, nor as to the distribution of morbidity by principal causes, such as is partly disclosed by an analysis of hospital experience.†

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* An earlier copy of this work was published in Philadelphia in 1793.

† The classification has since been adopted by many others.

The Registration of Diseases.—The first effort to bring about the registration of diseases appears to have occurred in 1855, when, at a meeting of the American Medical Association, held in Philadelphia, Dr. J. G. Orton, of Binghamton, N. Y., introduced a resolution providing that "It shall be the duty of each member of this Society to keep a faithful record of the diseases which may fall under his observation during each month, according to the classification adopted by this Convention, in May, 1847, stating the age and sex, occupation and nativity of the patient, the average duration of the disease, and, finally, recovery or death, and to report the same, in writing, to the Secretary, on or before the first day of February of each year, who shall transmit a digest thereof to the State Medical Society and, also, to the appropriate committee appointed by the American Medical Association for its reception."

The subject again came up for discussion as the result of an address before the American Medical Association, by Prof. A. B. Palmer, of Michigan University, at a meeting held in Detroit, in 1856. In 1858, Dr. Thomas E. Brinsmade, of Troy, submitted an elaborate report on his own experience, 1837-1857, inclusive, exhibiting in detail the causes, and the mortality from the several causes, classified according to accepted standards, with fatality rates worked out for each group of diseases and amplified by returns in detail by ages, months, etc. The discussion reveals many interesting facts, and, if continued to the present time, would disclose with accuracy the profound changes which have taken place in the morbidity and mortality of the city of Troy during the long intervening period. The total number of cases of sickness reported by the doctor during the period 1837-1847 was 8,195, the number of deaths was 344, and the resulting fatality rate was 4.2 per cent.

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* See article on "The German System of Compulsory Sickness Insurance," The Spectator, New York, Nov. 21, 1912.

† "Memorial to the President of the United States on the Appointment of a National Commission to Study the Subject of Occupational Diseases," published by The American Association for Labor Legislation, Jan., 1911.

In 1859, Dr. William C. Rogers, of Green Island, Albany Co., N. Y., contributed an interesting address on the registration of diseases to the transactions of the New York State Medical Society, which included a brief review of previous efforts in this direction in England, with references to remarks on the subject in the British Medical Almanac for 1837 and the British and Foreign Medical and Chirurgical Review for the same year.

A suggestive fact brought out by these extracts is the recognition of the value of hospital returns, properly classified, it being stated in part that "It is clear that the time is arriving when the medical officers of hospitals will find their best interests in rendering the facts which occur in these institutions as extensively useful as possible to the profession. System will enable them to offer these facts in the best form at the least trouble." (British and Foreign Medical and Chirurgical Review, 1837, p. 265.)

Notification of Infectious Diseases.—In 1876, Dr. F. W. Draper contributed an important paper on the registration of prevalent diseases, published in the annual report of the Massachusetts State Board of Health. Practically coincident with Dr. Draper's appeal, a more successful effort was made in the state of Michigan for the registration of infectious and other diseases, morbidity statistics having been collected by Michigan since that date. Of course, the registration of prevalent infectious diseases is but a first step toward the required universal notification of all important diseases, which it would seem can only be brought about by the coöperation of medical practitioners on the basis of the method suggested as early as 1855 by Dr. Orton, of Binghamton, New York.

Advantages of Publication of Hospital Experience.—Although the registration of deaths in the United States is now inclusive of about 63% of the total population, the registration of infectious diseases is still in a rather backward state. Until notification and registration become more general and comprehensive, the chief reliance for a study of American morbidity must be the statistics of institutions and of life and health insurance companies. The study of the subject would be immensely facilitated by the publication of hospital experience data on a uniform basis, with a due regard to the elements of the problem, as previously discussed. The present waste of these disease records is lamentable from every point of view, and the time may come when the collective experience of practising physicians will be required to establish the true incidence of sickness as it prevails throughout the country and as it is conditioned by local circumstances. But a consolidated report of hospital experience, for even a single city such as Baltimore, would be a genuine contribution to medical knowledge. If it is argued that such an effort would involve a considerable expenditure, it may be said that, in all probability, the cost would not be such a serious matter as is generally assumed, and that, in any event, hospital efficiency would be greatly increased and public appreciation of hospital treatment would be materially enhanced by a precise and conclusive statement of facts which are at present unobtainable.

Analysis of Population and Mortality Data.—In connection with a study of hospital experience data, it is necessary to take into account the factors of population, which vary sufficiently, in American cities, to affect the local hospital results. Having reference to the city of Baltimore, it appears that, according to the census of 1910, the total population of the city was returned as 558,485, of which 41.0 per cent were white males, 43.8 per cent white females, 7.0 per cent colored males and 8.2 per cent colored females. It is hardly necessary to point out that this population distribution of Baltimore is in marked contrast to the distribution of the population of a city like New York or Boston, where the proportion of negroes is materially less. The same conclusion holds true as regards the local death rate, and it may be stated in this connection that for the decade ending with 1911 the mortality of the white population of Baltimore was 17.8 per 1000, while for the colored population the death rate was 31.8, or 14.0 per 1000 in excess. The comparative death rates for tuberculosis were 17.0 per 10,000 for the white population, against

51.8 for the colored; for typhoid fever the death rate was 3.2 for the white population, against 4.3 for the colored; for cancer the death rate was 8.3 for the white population, against 6.5 for the colored; and for pneumonia the death rate was 14.9 for the white population, against 43.5 for the colored. These comparative rates indicate the material differences in the mortality of the white and colored population of Baltimore, and emphasize the necessity of differentiating, in hospital statistics, at least the factor of race and possibly the factor of nativity. The mortality rate, however, varies also according to sex; and this factor, perhaps more than any other, requires to be taken into account in hospital statistics, but, unfortunately, it is also one of the most neglected. According to the official statistics of Baltimore, the death rate from tuberculosis was 20.2 per 10,000 for the white male population, against 14.0 for white females; and 60.2 per 10,000 for the colored male population, against 44.6 for colored females. As regards cancer, the respective death rates were 6.4 per 10,000 for white males, against 10.1 for white females; and 3.7 per 10,000 for colored males, against 8.9 for colored females.

Admission of Non-Residents.—The experience of every hospital is more or less modified by the admission of non-resident patients. The statistics of The Johns Hopkins Hospital do not separate the resident from the non-resident patients, nor would this seem absolutely necessary for the general purposes of hospital reports. In an effort, however, to ascertain the relative admission rate, the results are likely to be materially impaired by the admission of non-residents, who, of course, cannot be accurately correlated to the local population. There are also no data on the subject of hospital admissions by local residence, but, in the official returns, the deaths in Baltimore institutions are classified according to residents and non-residents, and the following statement is of considerable value. It appears that during the decade ending with 1910 the institutional mortality of Baltimore was 16.7 per 10,000 for the resident white population and 32.6 for the resident colored. The proportion of deaths of non-residents was 7.0 per 10,000 for the white population and 8.3 for the colored. The institutional mortality of patients who were residents of the city of Baltimore was, therefore, almost exactly twice as high for the colored as for the whites. Of the total institutional mortality of the whites 70.5 per cent were residents of Baltimore, and of the colored, 79.7 per cent. Since non-resident patients usually represent the more serious cases, which are likely to be reflected in the hospital mortality, it is obvious that the proportion of non-resident patients should be stated in the general hospital returns, so that due allowance may be made for this fact in the subsequent interpretation of the data.*

Statistical Treatment of The Johns Hopkins Hospital Data.—As has been pointed out in the introductory discussion, the statistical treatment of hospital data is more difficult than is generally assumed, and particularly is this the case when the returns for single years are combined into a period of years. Naturally, at the beginning of each new year there are a number of patients carried forward from the previous year. This remnant, together with the number admitted during the current year, constitutes the "total number treated." In the case of a single year that would properly constitute the statistical basis for the calculation of recovery or mortality rates. When, however, these returns are combined, it is obvious that there would be duplications, in that the number remaining at the beginning of the year would be counted over and over again. Therefore, in calculating the admission and mortality rates for the decade, and with special reference to particular diseases or surgical operations, the proper statistical basis would appear to be the "number admitted" during each year, plus the number of patients remaining on hand at the beginning of the first year of the decade. This explanation seems necessary, since otherwise certain unavoidable differences in mortality rates may appear to be clerical errors or fallacies of statistical treatment. If the number remaining at the beginning of each year were excluded from the calculation of the rates for single years, and if such rates were calculated only from the number admitted during the year, it is self-evident that the rates would be too high. In any event, however, regardless of the methods adopted, the differences in the aggregate rates are not as a rule of material importance.

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* The details of the Baltimore hospital mortality rate, as derived from official returns, are as follows:

DEATHS IN HOSPITALS BY RESIDENCE, BALTIMORE, MD., 1901-1910.

	Aggregate Population.	Number of deaths.	Rate per 10,000 of population.
Resident whites	4,535,105	7,565	16.7
Non-resident whites	....	3,161	7.0
Resident colored	826,851	2,691	32.6
Non-resident colored	....	686	8.3

Limitations of Statistical Analysis.—The present general discussion of The Johns Hopkins Hospital data is limited to the 20-year period ending with January 31, 1912. Throughout, the distinction of race and sex is maintained in the returns, but the medical and surgical data in detail are considered only for the last decade, as a whole, since a treatment by single years would have unduly enlarged the present discussion, while probably adding little of material value to the results. The total number of male patients treated during the 20-year period was 41,026, and the total number of female patients was 41,399. In the first decade the males outnumbered the females, whereas in the last decade there was a slight excess of women patients. The number of male patients during the last decade exceeded by 25.3 per cent the number treated during the previous decade, whereas the number of female patients during the last decade increased by 39.8 per cent over the number of patients treated during the previous ten years. The tendency has, therefore, been towards a larger increase in the number and proportion of female patients during more recent years of hospital experience. The information in detail by single years is given in Table 1 of the Statistical Appendix.

Historical Review.—For a full understanding of the returns by single years, a brief historical account of the hospital during the last two decades would have been of value. It would carry me, however, entirely too far to enlarge upon this discussion at the present time. I have carefully read all of the reports, and, as a general conclusion, it may be stated that the financial difficulties through which the hospital has passed at different times are naturally reflected in the hospital accommodation and the number of patients treated.

Comparative Admission Rates by Race and Sex.—The average admission rate to The Johns Hopkins Hospital during the decade ending with 1911 was 81.8 per 10,000 of population of the city of Baltimore, carefully estimated on the revised results of the census, and for intercensal years.* In proportion to the white male population, the admission rate was 79.9 and to the white female population, 70.4. In proportion to the colored male population, the admission rate was 99.9, and to the colored female population, 135.4. How far these admissions are affected by other hospitals in Baltimore cannot be stated, since the information is not available as regards the total number of white and colored patients according to sex. It is evident, however, that in The Johns Hopkins Hospital there is a tendency to admit colored females in larger proportion than either colored males or white males or females, for it is shown that the admission rate for this group of patients was nearly twice the rate for white women. The facts in detail are given in the table below:

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* Upon the basis of such information as I have been able to secure, the total number of patients treated in the large hospitals of Baltimore during 1911 was about 20,000, which would be equivalent to an institutional admission rate (exclusive of dispensary cases) of 355 per 10,000 of population.

COMPARATIVE ADMISSION RATES, 1902-1911.

	Population.*	Admissions.	Rate per 10,000 of population.
White males	2,218,165	17,730	79.9
White females	2,365,045	16,657	70.4
Colored males	376,568	3,762	99.9
Colored females	451,700	6,114	135.4
	5,411,478	44,263	81.8

* For the ten years ending with 1911.

Comparative Admission Rates by Method of Treatment.—Differentiating the admission rates according to the four classes of cases admitted—that is, for males, whether medical or surgical, and for females, whether medical, surgical, obstetrical or gynecological—the following comparison is of considerable interest: The admission rate for white medical cases was 35.0 per 10,000 for males, but only 16.6 for females. The admission rate for white surgical cases was 44.9 for males, but only 16.2 for females. But, in addition, there was a white female admission rate of 27.2 for gynecological cases and of 10.5 for obstetrical cases. Combining medical, surgical, and other admissions, it appears that the total admission rate was 79.9 per 10,000 for white males, against 70.4 for white females.

Among the colored patients the admission rate for medical cases was 52.8 per 10,000 for males, against 21.8 for females. The admission rate for surgical cases was 47.1 for males, against 22.4 for females. In addition thereto, the admission rate for gynecological cases was 52.9, and for obstetrical cases 38.2. Combining the admissions for medical, surgical, and other causes, the total admission rate was 99.9 per 10,000 for colored males, against 135.4 for colored females.

Combining the sexes, the total admission rate was 75 per 10,000 for the white population, against 119 for the colored.

The facts in detail are given in the table below:

ADMISSIONS TO THE JOHNS HOPKINS HOSPITAL, 1902-1911.

	White.				Colored.			
	Males.		Females.		Males.		Females.	
Class of cases.	Admissions.	Rate per 10,000.	Admissions.	Rate per 10,000.	Admissions.	Rate per 10,000.	Admissions.	Rate per 10,000.
Medical	7,770	35.0	3,925	16.6	1,988	52.8	986	21.8
Surgical	9,960	44.9	3,821	16.2	1,774	47.1	1,013	22.4
Gynecological .	.....	...	6,426	27.2	.....	...	2,388	52.9
Obstetrical	.....	...	2,485	10.5	.....	...	1,727	38.2
Total	17,730	79.9	16,657	*70.4	3,762	99.9	6,114	*135.4

Admission Rates of Male Patients by Causes.—For the purpose of emphasizing more precisely the observed differences in the admission rates of white and colored patients, with distinction of sex, the following facts are presented, with the required brevity.

Considering first the male patients, it appears that for infectious diseases the white admission rate was 12.8 per 10,000, against a colored rate of 26.5. For digestive diseases, the white admission rate was 11.5, against a colored rate of 10.3. For diseases of the nervous system, the white rate was 6.8 per 10,000, against a colored rate of 3.0. For tumors, the white rate was 6.7 per 10,000, against a colored rate of 4.5. For injuries, the white rate was 6.5, against a colored rate of 8.3. For diseases of the circulatory system, the white rate was 5.3, against a colored rate of 15.4. For diseases of the reproductive organs, the white rate was 5.0, against a colored rate of 2.2. For all other causes, the white rate was 25.3 per 10,000, against a colored rate of 29.7.

The most important differences in the male admission rates are found in the excess of admissions of colored males on account of infectious diseases, injuries and circulatory diseases. An excess in the admission rate of white male patients over the colored is observed in the case of diseases of the digestive system, nervous system, tumors, and diseases of the reproductive organs.

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* Throughout the aggregate rates are the result of original calculations by division and do not represent the addition of the individual rates. In the present case the correct aggregate rates to the second decimal are 70.4 for white females and 135.4 for colored females, whereas the rates by simple addition would be 70.5 and 135.3, respectively.

In the case of certain special, or particular, diseases the following differences are suggestive:

For appendicitis, the white male admission rate was 3.8, against 2.3 for the colored. For syphilis, the white rate was 1.2, against 2.7 for the colored. For tuberculosis of the lungs, the white rate was 1.4, against 2.6 for the colored. For other forms of tuberculosis, the white rate was 2.3, against 9.0 for the colored. For typhoid fever, the white rate was 3.1, against a colored rate of 6.1. For lung diseases, the white rate was 1.5, against a colored rate of 7.3. For kidney diseases, the white rate was 2.6, against a colored rate of 3.0. With the exception, therefore, of appendicitis, the admission rate for all of the special, or particular, diseases, separately considered, was excessive for colored males, and particularly so in the case of other forms of tuberculosis, typhoid fever and non-tubercular diseases of the lungs.*

Admission Rates of Female Patients by Causes.—For female patients, the differences in the admission rates were as follows:

For infectious diseases, the white female admission rate was 5.3 per 10,000 of female population, against 13.2 for the colored. For digestive diseases, the white female admission rate was 7.2, against a colored rate of 9.8. For diseases of the nervous system, the white female admission rate was 5.1, against a colored rate of 2.1. For tumors, including cancers of all forms, the white female admission rate was 7.3, against a colored rate of 16.6. For injuries, the white rate was 1.5, against a colored rate of 2.4. For diseases of the circulatory system, the white rate was 1.3, against a colored rate of 3.7. For diseases of the reproductive organs, the white rate was 14.7, against a colored rate of 28.4. For obstetrical cases, the white rate was 12.6, against a colored rate of 41.4. For all other causes, the white rate was 15.4, against a colored rate of 17.8. With the exception, therefore, of diseases of the nervous system, the rates were in excess throughout for female colored patients, but particularly so in the case of infectious diseases, tumors, diseases of the reproductive organs and obstetrical cases.

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* The practice of the hospital with reference to the admission of tuberculosis patients is explained in the following official statement:

"We have no definite rule about the admission of tuberculosis patients. We do not generally admit open tuberculosis cases into our public wards, but have been obliged, from time to time, to receive such cases when there has been some complication which necessitated either active medical or surgical treatment. It is fair to state that the ordinary consumptive, to use common language, is not admitted at all to the hospital."

Considering some of the diseases in detail, the following facts are of interest:

For appendicitis, the white female admission rate was 2.9 against a colored rate of 2.1. For syphilis, the white rate was 0.3, against a colored rate of 1.5. For tuberculosis of the lungs, the white rate was 0.7 and the colored rate 1.7. For other forms of tuberculosis, the white rate was 1.5 and the colored rate 4.6. For typhoid fever, the white rate was 1.3 and the colored rate was 2.9. For lung diseases, the white rate was 0.4 and the colored rate 1.7. For kidney diseases, the white rate was 2.2 and the colored rate 1.9. With the exception, therefore, of appendicitis and kidney diseases, the admission rates were in excess for colored female patients, but particularly so in the case of syphilis, non-pulmonary tuberculosis, typhoid fever, and diseases of the lungs.

Comparative Admission Rates by Race, Sex and Cause.—For the purpose of convenient comparison, the facts are summarized in the following two tables:

COMPARATIVE ADMISSION RATES (PER 10,000 POPULATION), WHITE AND COLORED.

	Males.		Females.	
Causes.	White.	Colored.	White.	Colored.
Infectious diseases	12.8	26.5+	5.3	13.2+
Digestive diseases	11.5	10.3—	7.2	9.8+
Nervous diseases	6.8	3.0—	5.1	2.1—
Tumors	6.7	4.5—	7.3	16.6+
Injuries	6.5	8.3+	1.5	2.4+
Circulatory system	5.3	15.4+	1.3	3.7+
Reproductive organs	5.0	2.2—	14.7	28.4+
Obstetrical cases	...	...	12.6	41.4+
All others	25.3	29.7+	15.4	17.8+
Total	79.9	99.9+	70.4	135.4+

COMPARATIVE ADMISSION RATES (PER 10,000 POPULATION), SPECIAL CAUSES, WHITE AND COLORED.*

	Males.		Females.	
Special causes.	White.	Colored.	White.	Colored.
Appendicitis	3.8	2.3—	2.9	2.1—
Syphilis	1.2	2.7+	0.3	1.5+
Tuberculosis of lungs	1.4	2.6+	0.7	1.7+
Other tuberculosis	2.3	9.0+	1.5	4.6+
Typhoid fever	3.1	6.1+	1.3	2.9+
Lung diseases	1.5	7.3+	0.4	1.7+
Kidney diseases	2.6	3.0+	2.2	1.9—

Relative Admission Rates of White Female Patients.—Important variations in the admission rates are disclosed by an analysis of the separate causes, with the required distinction of sex and race. Since the facts are not available by divisional periods of life, a complete analysis is out of the question. The total admission rate for *white males* was 79.9 per 10,000 of population, while for white females the rate was 70.4. The admission rate for females was, therefore, 88 per cent of the male rate.

Considering the group of infectious diseases, the admission rate was 12.8 for males, against only 5.3 for females. The female admission rate was, therefore, only 41 per cent of the male rate.

For diseases of the digestive system, the male admission rate was 11.5, against a female admission rate of 7.2. The female admission rate was, therefore, 63 per cent of the male rate.

For diseases of the nervous system, the male admission rate was 6.8 per 10,000, against a female admission rate of 5.1. The female admission rate was, therefore, 75 per cent of the male rate.

For tumors, including under this term all tumors and cancers, whether benign or malignant, the admission rate for males was 6.7 per 10,000, against an admission rate of 7.3 for females. The female admission rate was, therefore, 109 per cent of the male rate.

For injuries, the male admission rate was 6.5 per 10,000, against a female admission rate of only 1.5. The female admission rate was, therefore, only 23 per cent of the male rate.

For diseases of the circulatory system, the male admission rate was 5.3 per 10,000, against a female admission rate of only 1.3. The female admission rate was, therefore, only 25 per cent of the male rate.

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* The plus and minus signs indicate the excess or deficiency, respectively, in the colored as compared with the white rates.

For diseases of the reproductive organs, the male admission rate was 5.0 per 10,000, against a female admission rate of 14.7. The female admission rate was, therefore, nearly three times the male rate.

For obstetrical cases, the admission rate was 12.6 per 10,000 of female population.

For all other causes and conditions, the male admission rate was 25.3 per 10,000, against a female admission rate of 15.4. The female admission rate for the group of all other causes, not conveniently admitting of a more extended discussion, was 61 per cent of the male rate.

Considering a few of the principal diseases in detail, the following are of special interest and importance:

For appendicitis, the male admission rate was 3.8 per 10,000, against a female admission rate of 2.9. The female admission rate for this disease was, therefore, 76 per cent of the male rate.

For syphilis, the male admission rate was 1.2 per 10,000, against a female admission rate of only 0.3. The female admission rate for this disease was, therefore, only 25 per cent of the male rate.

For tuberculosis of the lungs, the male admission rate was 1.4 per 10,000, against a female admission rate of only 0.7. The female admission rate for this disease was, therefore, 50 per cent of the male rate.

For other tubercular diseases, the male admission rate was 2.3 per 10,000, against a female admission rate of 1.5. The female admission rate for this group of diseases was, therefore, 65 per cent of the male rate.

For typhoid fever, the male admission rate was 3.1 per 10,000, against a female admission rate of 1.3. The female admission rate was, therefore, 42 per cent of the male rate.

For non-tubercular lung diseases, the male admission rate was 1.5 per 10,000, against a female admission rate of only 0.4. The female admission rate was, therefore, only 27 per cent of the male rate.

For kidney diseases, the male admission rate was 2.6 per 10,000, against a female admission rate of 2.2. The female admission rate was, therefore, only 85 per cent of the male rate.

According to this analysis, the relative admission rates were lower for females than for males for all specified diseases, with the exception of tumors and diseases of the reproductive organs. The most important variations are met with in the case of injuries, diseases of the circulatory system, syphilis and non-tubercular lung diseases. How far these differences are the result of selection, or custom and local usage, can, of course, not be stated. In other words, the results are probably not entirely conclusive as regards the true relative incidence of particular diseases among the two sexes, since for local, or hospital, reasons preference may be given to one sex or the other, in the admission for particular diseases, or causes, as the case may be.

Relative Admission Rates of Colored Female Patients.—The total admission rate for *colored males* was 99.9 per 10,000 of population, while for colored females the rate was 135.4. The admission rate for females was, therefore, 136 per cent of the male rate. (This is in contrast to a white female admission rate of only 88 per cent of the white male rate.)

Considering the group of infectious diseases, the admission rate was 26.5 for males, against 13.2 for females. The female admission rate was, therefore, 50 per cent of the male rate.

For diseases of the digestive system, the male admission rate was 10.3 against a female admission rate of 9.8. The female admission rate was, therefore, 95 per cent of the male rate.

For diseases of the nervous system, the male admission rate was 3.0 per 10,000, against a female admission rate of 2.1. The female admission rate was, therefore, 70 per cent of the male rate.

For tumors, including under this term all neoplasms, whether benign or malignant, the admission rate for males was 4.5 per 10,000, against an admission rate of 16.6 for females. The female admission rate was, therefore, 369 per cent of the male rate. (This is in curious contrast to the relative white female admission rate for tumors of only 109 per cent.)

For injuries, the male admission rate was 8.3 per 10,000, against a female admission rate of only 2.4. The female admission rate was, therefore, only 29 per cent of the male rate.

For diseases of the circulatory system, the male admission rate was 15.4 per 10,000, against a female admission rate of only 3.7. The female admission rate was, therefore, only 24 per cent of the male rate.

For diseases of the reproductive organs, the male admission rate was 2.2 per 10,000, against a female admission rate of 28.4. The female admission rate was, therefore, 1291 per cent or nearly thirteen times the male rate. (This, also, is in curious contrast to the relative white female admission rate for diseases of the reproductive organs of 294 per cent.)

For obstetrical cases, the admission rate was 41.4 per 10,000 of female population.

Considering a few of the principal diseases in detail, the following are of special interest and importance:

For appendicitis, the male admission rate was 2.3 per 10,000, against a female admission rate of 2.1. The female admission rate for this disease was, therefore, 91 per cent of the male rate.

For syphilis, the male admission rate was 2.7 per 10,000, against a female admission rate of 1.5. The female admission rate for this disease was, therefore, 56 per cent of the male rate. (In contrast, the relative white female rate for this disease was only 25 per cent.)

For tuberculosis of the lungs, the male admission rate was 2.6 per 10,000, against a female admission rate of 1.7. The female admission rate for this disease was, therefore, 65 per cent of the male rate.

For other tubercular diseases, the male admission rate was 9.0 per 10,000, against a female admission rate of 4.6. The female admission rate for this group of diseases was, therefore, 51 per cent of the male rate.

For typhoid fever, the male admission rate was 6.1 per 10,000, against a female admission rate of 2.9. The female admission rate was, therefore, 48 per cent of the male rate.

For non-tubercular lung diseases, the male admission rate was 7.3 per 10,000, against a female admission rate of 1.7. The female admission rate was, therefore, only 23 per cent of the male rate.

For kidney diseases, the male admission rate was 3.0 per 10,000, against a female admission rate of 1.9. The female admission rate was, therefore, 63 per cent of the male rate.

The conclusions, as regards the sex differences in the admission rates for the colored population, are practically the same as for the whites. The most suggestive difference is found in the enormous disproportion of admissions of colored females for diseases of the reproductive organs, equivalent to 1291 per cent of the male admission rate. A very substantial difference also exists in the admission rates for tumors, which, in the case of colored females, show an admission rate of 369 per cent of the colored male admission rate. As in the case of white admissions, the lowest relative rates for women are met with in the case of injuries and diseases of the circulatory system, and also in the case of non-tubercular diseases of the lungs.

How far these differences are the result of selection, etc., cannot be stated.

Statistical Basis of Hospital Efficiency.—Qualified opinion differs as regards the most conclusive test of hospital efficiency. Perhaps no single test meets all modern requirements, but it has seemed best to limit the present considerations to the death rate. In view of the fact that in The Johns Hopkins Hospital statistics the number of patients "recovered and improved" is combined, it is evident that for medical purposes no precise conclusions can be based upon this term. The term "unimproved" is also subject to a certain degree of indefiniteness, but the number of such cases is relatively small, so that the resulting percentages would not be of much practical value. The number "not treated" is an additional indefinite element which, it would seem, should be reduced to the lowest possible minimum. This group probably represents patients admitted, but subsequently found unsuitable for hospital treatment, or not in need thereof. The number "transferred" is also relatively small, and since the reasons for transfers are not given, the group cannot be dealt with to practical advantage. The deaths, however, are a precisely defined and self-limited group, which, while comparatively small, yet represents, from the medical and hospital points of view, the most important test of institutional efficiency. In what follows, therefore, the discussion is practically limited to the mortality percentage, by groups of diseases and single causes, the percentage, unless otherwise stated, being based upon the total number admitted during the decade ending with 1911 and the total number of deaths during the same period.* The only exceptions to this rule are the first 23 tables, in which the rates are calculated upon the number treated, for reasons explained in the introduction. By limiting the discussion of the mortality by groups of diseases and single causes to a ten-year period, a much larger and more trustworthy basis of facts is secured, so that accidental fluctuations in the results are, as far as practicable, eliminated.

Comparative Mortality Rate, 1902-1911.—The aggregate experience of The Johns Hopkins Hospital during the decade ending with Jan. 31, 1912, includes 22,819 male and 24,138 female patients. The average mortality rate, as determined on the basis of the total number of patients "treated," was 7.6 per cent for males and 4.1 per cent for females. During the preceding decade the male mortality rate was

* See page 11 for full explanation.

7.8 per cent and the female rate 5.1 per cent. The range in the male mortality rate has been from a maximum of 8.9 per cent during 1901-1902 to a minimum of 6.1 per cent during 1910. The maximum mortality rate for female patients occurred in 1892, when it was 6.0 per cent, and the minimum rate occurred in 1908, when it was only 2.9 per cent.

Comparative Mortality Rate by Race and Sex.—Throughout the entire experience, the mortality rate of colored patients has been higher, and for both sexes, than the corresponding death rate of white patients. During the last decade, it appears that the white male death rate was 6.6 per cent, while for the colored patients it was 12.6 per cent; for white female patients the death rate was 3.6 per cent, against 5.3 per cent for colored female patients. The maximum colored mortality rate for males occurred in 1901, when it reached 14.4 per cent; the minimum rate occurred in 1910, when it was 9.1 per cent. The lowest rate for colored male patients, however, was still considerably in excess of the maximum mortality rate for white male patients. The maximum death rate for colored females occurred in 1892, when it reached 14.3 per cent, and the minimum rate occurred in 1908, when it was 3.8 per cent. The differences in the mortality rates of white and colored males are, therefore, much more pronounced than in the case of white and colored females, but practically throughout, the female death rates for colored patients have been considerably in excess of the corresponding rates for white female patients. A general summary of the facts is given in the table below, for the ten years ending with 1911:

COMPARATIVE DEATH RATES, WHITE AND COLORED, THE JOHNS HOPKINS HOSPITAL, 1902-1911.

Patients.	Total number treated.	Total number of deaths.	Mortality percentage.
White patients:			
Males	18,792	1,235	6.6
Females	17,675	637	3.6
Total whites	36,467	1,872	5.1
Colored patients:			
Males	4,027	509	12.6
Females	6,463	342	5.3
Total colored	10,490	851	8.1
Total, white and colored	46,957	2,723	5.8

Variations in Methods of Statistical Treatment of Hospital Data.—The foregoing mortality rates, however, require to be considered with caution, since they differ slightly from the rates subsequently to be given on the basis of the patients "admitted." For reasons previously explained, this difference cannot be eliminated from the present discussion, in which the returns for a series of years have been combined into a group. Since the number admitted is always less than the number treated, which includes the number remaining from the previous year, the rates based on the number "admitted" are, therefore, slightly higher throughout than the rates based on the number "treated."

Variations in Death Rate According to Class of Patients Treated.—The death rate has varied considerably, according to the class of patients treated, whether medical, surgical, gynecological or obstetrical. In the experience of The Johns Hopkins Hospital the death rate was highest during the decade under review among colored male medical cases, or 16.2 per cent, and lowest for colored obstetrical cases, or only 1.5 per cent.

Comparative Mortality Rates of White Patients by Sex.—The comparative mortality rates of white patients are given in tabular form below:

COMPARATIVE MORTALITY RATES,* WHITE PATIENTS, 1902-1911.

	Males.			Females.		
Class of cases.	Treated.	Number of deaths.	Percentage.	Treated.	Number of deaths.	Percentage.
Medical	8,213	624	7.6	4,186	223	5.3
Surgical	10,579	611	5.8	4,054	223	5.5
Gynecological	......	....	..	6,803	141	2.1
Obstetrical	......	....	..	2,632	50	1.9
Total	18,792	1,235	6.6	17,675	637	3.6

* On the basis of the number of patients treated. The diagram opposite exhibits the fatality rates on the basis of the number admitted.

Variations in Mortality Rates According to Race and Sex.—This comparison conclusively proves the importance of differentiating in hospital statistics the mortality rates of the different classes of patients. It may, therefore, be laid down as an axiom that the general hospital death rate is misleading unless corrected for sex and race and the kind of treatment—that is, medical, surgical, etc.

Comparative Mortality Rates of Colored Patients by Sex.—For colored patients the facts in detail are given in tabular form below:

COMPARATIVE MORTALITY RATES,* COLORED PATIENTS, 1902-1911.

	Males.			Females.		
Class of cases.	Treated.	Number of deaths.	Percentage.	Treated.	Number of deaths.	Percentage.
Medical	2,109	342	16.2	1,046	166	15.9
Surgical	1,918	167	8.7	1,073	79	7.4
Gynecological	....	....	..	2,504	69	2.8
Obstetrical	....	....	..	1,840	28	1.5
Total	4,027	509	12.6	6,463	342	5.3

* On the basis of the number of patients treated.

According to this table, the death rate of colored male medical cases was 16.2 per cent, against 8.7 per cent for surgical cases. For females, the respective percentages were 15.9 and 7.4. For colored gynecological cases, the death rate was 2.8, and for obstetrical cases, 1.5 per cent.

*Mortality Rate by Divisional Periods of Life.**—On account of the required brevity, the fluctuations in the medical and surgical, as well as the gynecological and obstetrical, death rates, by single years, cannot be discussed. All the facts are given in full in Tables 2-12 of the Statistical Appendix, for the white patients, and Tables 13-23 for the colored. The same conclusion also applies to the consideration of the mortality by divisional periods of life, which, however, cannot be extended to causes of admission, since these facts are only given for all patients, considered as a group.

Comparative Mortality by Age, Race and Sex.—The facts, in some detail, are given in the table below, but the data in full are given in the Statistical Appendix in Tables 6-12 for the white patients, and in Tables 17-23 for the colored patients.

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* The table below emphasizes the importance of giving the hospital admissions by causes with the distinction of age and sex. In the case of many diseases the fatality rate varies considerably according to age and this is particularly true, of course, for the acute infectious diseases of infancy and childhood. That these differences are considerable and important is

COMPARATIVE MORTALITY * BY AGE.

Ages.	White. Males.	White. Females.	Colored. Males.	Colored. Females.
Under 15	8.9	9.3	11.0	11.6
15-24	3.5	2.0	10.3	2.4
25-34	4.6	2.1	11.8	3.8
35-44	6.4	3.6	13.7	8.7
45-54	8.0	5.5	16.5	13.5
55-64	9.3	7.3	14.7	14.4
65 and over	11.0	8.4	16.5	23.3

* Rates calculated on the number of patients treated.

It is shown by the above summary table that the mortality rate was relatively high at ages under 15, or, respectively, 8.9 per cent for white male patients, and 9.3 per cent for white female patients, and 11.0 per cent and 11.6 per cent, respectively, for colored males and females. The mortality rate decreased during the next decade of life, increasing subsequently from decade to decade, and reaching a maximum for both races at ages 65 and over. The range in the mortality rates, however, was much less for colored males, and throughout life the death rates for the colored were considerably in excess of the corresponding death rates for the white patients.

clear from the following statistics compiled from the Reports of the Metropolitan Asylums Board, London, Eng.

COMPARATIVE MORTALITY FROM SPECIFIED ACUTE INFECTIOUS DISEASES, BY SEX AND AGE, METROPOLITAN ASYLUMS BOARD, LONDON, ENG., 1910-1911.

Ages.	Diphtheria. Admitted.	Diphtheria. Died.	Diphtheria. Per cent.	Scarlet Fever. Admitted.	Scarlet Fever. Died.	Scarlet Fever. Per cent.	Measles. Admitted.	Measles. Died.	Measles. Per cent.	Whooping Cough. Admitted.	Whooping Cough. Died.	Whooping Cough. Per cent.
Males.												
Under 5	1,854	214	11.5	2,727	139	5.1	1,362	239	17.5	543	69	12.7
5-9	1,502	92	6.1	3,491	49	1.4	297	8	2.7	56	1	1.8
10-19	571	12	2.1	1,649	17	1.0	31	1	3.2	1	..	...
20-over	167	3	1.8	417	5	1.2	8	...	...	...	..	...
All Ages	4,094	321	7.8	8,284	210	2.5	1,698	248	14.6	600	70	11.7
Females.												
Under 5	1,792	228	12.7	2,718	102	3.8	1,335	217	16.3	579	71	12.3
5-9	1,775	135	7.6	4,050	46	1.1	363	11	3.0	67	4	6.0
10-19	704	19	2.7	1,905	16	0.8	31	..	..	2	..	...
20-over	303	6	2.0	643	6	0.9	14	...	...	...	..	...
All Ages	4,574	388	8.5	9,316	170	1.8	1,743	228	13.1	648	75	11.6

I am not aware of any corresponding information for other public or private hospitals of the United States, although as here shown the age factor is of considerable importance in determining the general death rate. Obviously, a hospital admitting a disproportionately large number of patients at ages 15-34, when the death rate is relatively low, must have a more favorable general death rate, without necessarily any reference to the true results of institutional treatment, than a hospital admitting an unduly large proportion of patients at ages under 15 or over 35, when the specific death rates, by divisional periods of life, are above the average for all ages.

Percentage Distribution of Causes of Admission, White Patients.—In the concluding discussion of the mortality, by groups of diseases, or special causes, the mortality percentage is always determined on the basis of the number of "admissions." Before considering the mortality rate by diseases in detail, however, it will serve a useful purpose to point out briefly the percentage distribution of principal causes of hospital admission , with a due regard to sex and race. Among white male patients, 16.0 per cent of the morbidity was due to infectious diseases, 14.4 per cent to diseases of the digestive system, and 8.6 per cent to diseases of the nervous system. These three groups of causes, therefore, accounted for 39.0 per cent of the morbidity from all causes. The ten specified causes given in the following table accounted for 83.1 per cent of the morbidity from all causes. Among the white female patients the principal cause of morbidity was diseases of the reproductive organs, or 20.8 per cent of the morbidity from all causes. The next most important group of disorders was obstetrical conditions, or 17.8 per cent, followed by cancers and tumors, with 10.4 per cent. These three groups of disorders, therefore, accounted for 49.0 per cent of the morbidity from all causes. The ten specified groups of causes, according to the table below, accounted for 84.8 per cent of the morbidity from all causes. Among other interesting facts, it is shown, by this comparison, that diseases of the reproductive functions * are of predominating importance among women, whereas, among white male patients, injuries are of the fifth order of importance, accounting for 8.1 per cent of the morbidity † from all causes, against 2.1 per cent for female patients. Another significant feature of the morbidity of white male patients is the relative frequency of hernia, accounting for 5.1 per cent of the morbidity from all causes. The details for white patients are given in the table following:

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* In hospital experience.

† The term morbidity is here used in a general sense and includes injuries as well as diseases and non-pathalogical reasons for admission.

PERCENTAGE DISTRIBUTION OF MORBIDITY OF PATIENTS ADMITTED TO THE JOHNS HOPKINS HOSPITAL, 1902-1911.

WHITE PATIENTS.

Males.		Females.	
Causes.	Percentage.	Causes.	Percentage.
Infectious diseases	16.0	Reproductive organs	20.8
Digestive system	14.4	Obstetrical conditions	17.8
Nervous system	8.6	Cancers and tumors	10.4
Cancers and tumors	8.4	Digestive system	10.3
Injuries	8.1	Infectious diseases	7.6
Circulatory system	6.6	Nervous system	7.2
Reproductive organs	6.2	Urinary system	4.5
Hernia	5.1	Ductless glands and spleen	2.4
Urinary system	5.0	Injuries	2.1
Respiratory system	4.7	Respiratory system	1.7
Total for ten causes	83.1	Total for ten causes	84.8
All other causes	16.9	All other causes	15.2
Total, all causes	100.0	Total, all causes	100.0

Percentage Distribution of Causes of Admission, Colored Patients.—Among colored male patients infectious diseases were of the first order of importance, accounting for 26.5 per cent of the morbidity from all causes. The next most important group of diseases was disorders of the circulatory system, accounting for 15.4 per cent, followed by disorders of the respiratory system, with 10.4 per cent. The morbidity from injuries was 8.3 per cent, or about the same as for white male patients (8.1 per cent); but in marked contrast to white male patients, the morbidity from hernia was not among the ten leading causes, but may here be referred to as having been 3.5 per cent (5.1 per cent for white male patients). Among colored females, obstetrical conditions come first, with 30.6 per cent, followed by disorders of the reproductive organs, with 21.0 per cent. The two causes combined account for 51.6 per cent of the morbidity from all causes, against 38.6 per cent for white females. Cancers and non-malignant tumors hold third place in the morbidity list for colored females, or the same position as for white females, but the percentage was 12.2 for the colored, against 10.4 for white females. The details for colored patients are given in the following table:

PERCENTAGE DISTRIBUTION OF MORBIDITY OF PATIENTS ADMITTED TO THE JOHNS HOPKINS HOSPITAL, 1902-1911.

COLORED PATIENTS.

Males.		Females.	
Causes.	Percentage.	Causes.	Percentage.
Infectious diseases	26.5	Obstetrical conditions	30.6
Circulatory system	15.4	Reproductive organs	21.0
Respiratory system	10.4	Tumors	12.2
Digestive system	10.3	Infectious diseases	9.8
Injuries	8.3	Digestive system	7.2
Urinary system	5.3	Circulatory system	2.7
Tumors	4.5	Urinary system	2.3
Nervous system	3.0	Respiratory system	2.2
Reproductive organs	2.2	Injuries	1.8
Bones, etc.	2.1	Nervous system	1.5
Total for ten causes	88.0	Total for ten causes	91.3
All other causes	12.0	All other causes	8.7
Total, all causes	100.0	Total, all causes	100.0

Summary Comparison of Admissions by Race and Sex.—According to these tables the four principal groups of causes accounted for 47.1 per cent of the admissions of white male patients, for 59.3 per cent of white females, for 62.6 per cent of the admissions of colored males, and for 73.6 per cent of colored females. At the risk of repetition, the more important facts are set forth in tabular form, as follows:

SUMMARY OF PERCENTAGE DISTRIBUTION OF ADMISSIONS BY PRINCIPAL CAUSES, ACCORDING TO RACE AND SEX, 1902-1911.

Principal causes.	Percentage of total Admissions.
White males:	
Infectious diseases	16.0
Digestive system	14.4
Nervous system	8.6
Injuries	8.1
	47.1
White females:	
Reproductive organs	20.8
Obstetrical conditions	17.8
Tumors	10.4
Digestive system	10.3
	59.3

SUMMARY OF PERCENTAGE DISTRIBUTION OF ADMISSIONS BY PRINCIPAL CAUSES, ACCORDING TO RACE AND SEX, 1902-1911—Continued.

Principal causes.	Percentage of total Admissions.
Colored males:	
Infectious diseases	26.5
Circulatory system	15.4
Respiratory system	10.4
Digestive system	10.3
	62.6
Colored females:	
Obstetrical conditions	30.6
Reproductive organs	21.0
Tumors	12.2
Infectious diseases	9.8
	73.6

Additional details regarding causes of admission will be found, for white patients, in Tables 30-33 of the Statistical Appendix, and for colored patients, in Tables 34-37, inclusive.

Mortality Rate by Groups of Causes and Selected Diseases, White Patients.—Considering first the white patients only, but with distinction of sex, and according to all classes of cases, that is, medical or surgical, gynecological or obstetrical, it is shown by Tables 38-41 of the Statistical Appendix that there are many important variations in the death rate, of which the following are given as interesting illustrations:

The mortality rate in diseases of the circulatory system was 14.4 per cent for white males, against 14.0 per cent for white females. In the group of diseases of the digestive system, the mortality rates were 5.3 for males and 3.4 for females. In diseases of the ductless glands and spleen, the mortality rate was 5.9 per cent for males, against 3.0 per cent for females. In diseases of the ear, the rates were 7.3 for males and 3.6 for females. The rates for infective diseases were 6.0 per cent for males and 5.9 per cent for females. In hernia the mortality rate for males was 2.0 per cent, but for females it was 6.1 per cent. In diseases of the nervous system, the death rate was 4.5 per cent for males, against only 1.9 per cent for females; but, considering separately diseases of the brain and spinal cord, the death rate for males was 17.5 per cent, against 13.6 per cent for females. In diseases of the reproductive organs the male death rate was 4.1 per cent, against a female death rate of only 1.2 per cent. In diseases of the respiratory system the male death rate was 10.7 per cent against 8.6 per cent for females. In the case of tumors, both benign and malignant, the male death rate was 13.7 per cent, and the female death rate 8.3 per cent. Considering benign tumors separately, the male death rate was 10.5 per cent and the female death rate 5.2 per cent. In the case of malignant tumors the male death rate was 15.0 per cent and the female death rate 10.7 per cent. In the group of diseases of the urinary organs the male death rate was 11.4 per cent and the female rate 5.5 per cent. For obstetrical conditions of all kinds, subsequently to be considered in some detail, the death rate for white females was 2 per cent. For injuries the male death rate was 5.6 per cent, but the female death rate was more than twice as high, or 11.7 per cent.

Table of Admissions and Mortality by Selected Causes, White Males.—The following table will show in some detail, for white males, the mortality from certain specified causes, represented by more than 500 admissions:

ADMISSIONS AND MORTALITY BY SELECTED CAUSES, 1902-1911.

WHITE MALES.

Selected causes.	Number of admissions.	Number of deaths.	Percentage.
Arteries, veins	615	74	12.0
Appendicitis	840	29	3.5
Rectum, anus	513	4	0.8
Typhoid fever	695	52	7.5
Hernia	903	18	2.0
Functional nervous diseases	1,015	4	0.4
Prostate gland	767	43	5.6
Malignant tumors	1,059	159	15.0
Kidney diseases	575	83	14.4
Injuries	1,436	80	5.6

NOTE.—This table includes all causes represented by more than 500 admissions.

Table of Admissions and Mortality by Selected Causes, White Females.—In a similar manner, the mortality of white females has been tabulated with reference to diseases represented by more than 250 admissions:

ADMISSIONS AND MORTALITY BY SELECTED CAUSES, 1902-1911.

WHITE FEMALES.

Selected causes.	Number of admissions.	Number of deaths.	Percentage.
Appendicitis	678	8	1.2
Gall bladder and duct	311	15	4.8
Thyroid gland	368	11	3.0
Tuberculosis (non-pulmonary)	353	29	8.2
Typhoid fever	307	18	5.9
Diseases of the joints	265	2	0.8
Diseases of the mind	274	1	0.4
Functional nervous diseases	913	3	0.3
Functional diseases of reproductive organs	624	1	0.2
Ligaments, tubes, ovaries	1,256	27	2.1
Uterus	856	4	0.5
Vagina	611	7	1.1
Benign tumors	750	39	5.2
Malignant tumors	981	105	10.7
Diseases of the kidneys	521	40	7.7
Obstetrical conditions	2,973	59	2.0
Injuries	350	41	11.7

NOTE.—This table includes all causes represented by more than 250 admissions.

Table of Admissions and Mortality by Selected Causes, Colored Patients.—The morbidity distribution for colored patients is somewhat less varied than for the whites, but the mortality differences for the two sexes are equally pronounced. For diseases of the circulatory system the mortality was 19.1 per cent for colored males, against 21.8 per cent for colored females. For diseases of the digestive system the respective death rates were 8.0 per cent for males and 9.3 per cent for females. For infectious diseases the mortality percentages were 14.4 for males and 10.2 for females. For diseases of the nervous system the male mortality percentage was 18.7 and the female 29.8. Considering diseases of the brain and spinal cord separately, the mortality rate for males was 33.3 per cent, against 55.8 per cent for females. For diseases of the reproductive organs the mortality was 14.8 per cent for males, against only 1.3 per cent for females. For diseases of the respiratory system the death rate for males was

17.9 per cent, against 21.2 per cent for females. For tumors, both benign and malignant, the mortality percentage was 20.0 for males, against 6.0 for females. Considering benign tumors separately, the mortality rates were 5.9 per cent for males, against 4.0 per cent for females. For malignant tumors the death rate was 26.1 per cent for males, against 11.3 per cent for females. For diseases of the urinary organs the mortality was 17.5 per cent for males, against 13.6 per cent for females. For obstetrical conditions the colored female mortality rate was 1.6 per cent. For injuries the male mortality rate was 4.5 per cent and the female rate 14.0 per cent.

The following table will show in some detail, for colored males, the principal causes of admission, represented by more than 200 admissions:

ADMISSIONS AND MORTALITY BY SELECTED CAUSES, 1902-1911.

COLORED MALES.

Selected causes.	Number of admissions.	Number of deaths.	Percentage.
Arteries, veins	316	60	19.0
Endocardium	214	44	20.6
Tuberculosis (non-pulmonary)	340	56	16.5
Typhoid fever	231	29	12.6
Diseases of the lungs	274	61	22.3
Injuries	312	14	4.5

NOTE.—This table includes all causes represented by more than 200 admissions.

The table which follows gives the same information for colored females, but only for causes represented by more than 100 admissions:

ADMISSIONS AND MORTALITY BY SELECTED CAUSES, 1902-1911.

COLORED FEMALES.

Selected causes.	Number of admissions.	Number of deaths.	Percentage.
Rectum and anus	124	4	3.2
Tuberculosis (non-pulmonary)	209	22	10.5
Typhoid fever	129	12	9.3
Ovaries, tubes	953	15	1.6
Uterus	123	..	...
Benign tumors	545	22	4.0
Malignant tumors	203	23	11.3
Obstetrical	1,868	30	1.6
Injuries	107	15	14.0

NOTE.—This table includes all causes represented by more than 100 admissions.

Observations on Possible Errors in Disease Classification.—On account of the required brevity, a discussion in detail of the mortality percentages for medical, surgical, gynecological and obstetrical cases has to be omitted. All the facts are given in full in Tables 42, 43, 44 and 50, 51 and 52 of the Statistical Appendix. The diseases in these tables have been arranged alphabetically, as given in the annual reports of The Johns Hopkins Hospital. For some purposes, however, the summary tables will be more useful than the others. Since the precise meaning of medical and surgical cases cannot always be given, it is obvious that for certain purposes these cases require to be combined, and the same holds true of gynecological cases, also. In the alphabetical arrangement of the causes of admission, I have combined many equivalent terms which were separately given in the orginal reports, such for illustration as whooping cough and pertussis, etc. Such needless and confusing repetitions are entirely avoided by the use of the Bellevue classification.

Comparative Mortality in Medical and Surgical Cases.—The comparative mortality rate in medical and surgical cases, due to the same disease, is, of course, a matter of special interest from a medical and surgical point of view. For the present purpose the comparison is necessarily limited to a few typical illustrations, and, unless otherwise stated, the observations have reference to white patients only.

In typhoid fever the mortality rate in white male medical cases was 4.4 per cent, against 59.0 per cent for surgical cases. For white females the percentage was 4.8 for medical cases, against 36.4 for surgical cases, but it should be understood that the actual number of surgical typhoid fever cases was relatively small.

Comparative Mortality, Medical and Surgical, in Appendicitis.—In appendicitis the mortality rate in medical cases was 2.3 per cent for white males, against a surgical mortality rate of 3.5 per cent. For white females the mortality rate was *nil* in medical cases and only 1.5 per cent in surgical cases. On account of the medical and surgical significance of this disease, I give the facts for both the white and the colored patients in tabular form, as follows:

MORTALITY RATE IN APPENDICITIS, THE JOHNS HOPKINS HOSPITAL, 1902-1911.

	Males.			Females.		
Class of cases.	Number of admissions.	Number of deaths.	Percentage.	Number of admissions.	Number of deaths.	Percentage
		WHITE PATIENTS.				
Medical	44	1	2.3	42	..	...
Surgical	796	28	3.5	410	6	1.5
Gynecological	...	..	..	226	2	0.9
Total	840	29	3.5	678	8	1.2
		COLORED PATIENTS.				
Medical	5	1	20.0	5	..	...
Surgical	80	9	11.3	50	7	14.0
Gynecological	...	..	..	40	3	7.5
Total	85	10	11.8	95	10	10.5

This table, in addition to the medical and surgical cases, gives also, for both white and colored women, the gynecological cases complicated by appendicitis. The relatively high mortality rates for the colored are of special significance.

For diseases of the stomach the mortality rate in white male medical cases was 0.6 per cent, against 11.8 per cent in surgical cases. For white females the respective mortality rate was *nil* for medical cases and 21.1 per cent for surgical cases.

For syphilis the mortality rate was 2.0 per cent in white male medical cases, against 2.9 per cent in surgical cases.

For tuberculosis of other forms (excluding tuberculosis of the lungs, tuberculosis of the meninges, and miliary tuberculosis), the mortality rate of white males was 17.9 per cent for medical cases, and 2.5 per cent for surgical cases. The corresponding mortality rates for white females were 17.4 per cent for medical cases, 2.1 per cent for surgical cases, and 5.9 per cent for gynecological cases.

For diseases of the brain and spinal cord the mortality rates were 13 per cent for white male medical cases and 23.7 per cent for surgical cases. The corresponding mortality rates for white females were 12.7 per cent for medical cases and 14.5 per cent for surgical cases.

For diseases of the reproductive organs the mortality rates for white males were 4.2 per cent for medical cases and 4.1 per cent for surgical cases. The corresponding mortality rates for white females were *nil* for medical cases, 1.8 per cent for surgical cases, and 1.1 per cent for gynecological cases.

For diseases of the respiratory system the mortality rates for white males were 11.7 per cent for medical cases and 7.1 per cent for surgical cases. The corresponding rates for white females were 10.4 per cent for medical cases, 2.9 per cent for surgical cases, and *nil* for obstetrical cases.

Comparative Mortality, Medical and Surgical, in Tumors.—For tumors the facts are of such exceptional interest that the information is given in tabular form below, according to sex and race, with distinction of benign and malignant tumors, subsequently to be discussed in more detail:

MORTALITY RATE IN TUMORS, THE JOHNS HOPKINS HOSPITAL, 1902-1911.

Class of cases.	Males.			Females.		
	Number of admissions.	Number of deaths.	Percentage.	Number of admissions.	Number of deaths.	Percentage.
BENIGN TUMORS, WHITE PATIENTS.						
Medical	65	5	7.7	44	5	11.4
Surgical	372	41	11.0	218	19	8.7
Gynecological	...	..	..	488	15	3.1
Total	437	46	10.5	750	39	5.2
MALIGNANT TUMORS, WHITE PATIENTS.						
Medical	256	38	14.8	93	14	15.1
Surgical	803	121	15.1	485	46	9.5
Gynecological	...	..	..	403	45	11.2
Total	1059	159	15.0	981	105	10.7
BENIGN TUMORS, COLORED PATIENTS.						
Medical	11	1	9.1	16	2	12.5
Surgical	40	2	5.0	47	1	2.1
Gynecological	...	..	..	482	19	3.9
Total	51	3	5.9	545	22	4.0
MALIGNANT TUMORS, COLORED PATIENTS.						
Medical	37	8	21.6	13	3	23.1
Surgical	82	23	28.0	88	8	9.1
Gynecological	...	..	..	102	12	11.8
Total	119	31	26.1	203	23	11.3

These tables are self-explanatory and require no extended discussion. The results are rather conflicting and not entirely conclusive. For illustration, the mortality rate in benign tumors was 7.7 per cent for white medical cases, against 11.0 per cent for surgical cases; but for white females the mortality rate for medical cases was 11.4 per cent, against 8.7 per cent for surgical cases and 3.1 per cent for gynecological cases. For malignant tumors the mortality rate for white male medical cases was 14.8 per cent, against 15.1 per cent for surgical cases; but the corresponding rates for white females were 15.1 per cent for medical cases, 9.5 per cent for surgical cases, and 11.2 per cent for gynecological cases. Some interesting contrasts are presented in the white and colored mortality rates, but these cannot be discussed here in detail. Nor is it possible, on account of the required brevity, to enlarge upon the mortality rate in the different forms of cancer, which, however, are given in full detail in the alphabetical tables of the Statistical Appendix (Tables 42-44 and 50-52).

Special Statistics of Admission and Mortality, Malignant Tumors.—To facilitate the study of the statistics of malignant tumors, I have abstracted the same from the annual reports, separately, by single years. The facts are given in detail in Tables 54-57 of the Statistical Appendix, together with the admission rates per 10,000 of population, and the mortality rates according to color and sex. Having reference only to the death rate, it is shown that for all cases of malignant tumors combined, the rate has remained practically the same for white patients, but for colored patients the rate has increased for males, but decreased considerably for females. The admission rates for malignant tumors have increased for white male patients from 4.1 to 4.8 per 10,000 of population, comparing the last ten years with the previous decade, but the admission rates decreased for white female patients from 5.8 to 4.2. For colored male patients the admission rates have increased from 2.3, during the first decade, to 3.2 during the last, but for colored females the admission rates increased only from 4.1 to 4.5.

As shown in the preceding table, the number of admissions of female colored patients for benign tumors has largely exceeded the admissions for malignant tumors, or, to be precise, the former numbered 545 during the last decade, against 203 for the latter. In contrast, the number of white females admitted for malignant tumors considerably exceeded the number of patients admitted for benign tumors, or, to be precise, the former numbered 981, against 750 for the latter. In the case of both white and colored males the number of admissions for malignant tumors far exceeded the number of admissions for benign tumors, but at present no explanation can be given for these rather curious, though interesting, differences in the tumor admission rates, according to color and sex.

Comparative Mortality in Medical and Surgical Cases of Injuries. The discussion of the comparative mortality of medical and surgical cases must here be concluded by a brief reference to injuries. For white males the mortality rate in injury cases was 5.3 per cent for medical cases, against 5.6 per cent for surgical cases. The corresponding mortality rate for females was *nil* for medical cases, but 12 per cent for surgical cases.

Comparative Mortality in Colored Medical and Surgical Cases.—It would not seem necessary to discuss in similar detail the comparative mortality of colored medical and surgical cases, except as has been done in the tabular presentation of the experience data for appendicitis and tumors. As has been pointed out, the terms medical and surgical are not precisely defined, and it is quite possible that serious medical cases have been reported as surgical, merely because of some simple, but necessary, surgical operation. It would be a most useful contribution to medical knowledge if a better definition of these terms were adopted, if only as an aid to a more satisfactory statistical classification.

Mortality Rate in Gynecological and Obstetrical Cases.—To a certain extent, the same conclusion applies to gynecological cases, which, as shown by the tables, include a large variety of diseases and complications, not necessarily peculiar to the sex. For obstetrical cases, however, I have prepared two special tables, showing details of special interest and importance. The tables are self-explanatory and require no extended discussion. For white patients the mortality rate in cases of operative labor was 4.5 per cent, while for colored patients the rate was 6.9 per cent. For spontaneous and premature labor the mortality rate was 1.8 per cent for white patients, against 2.7 per cent for colored. In further contrast, however, in cases admitted in a post-partum condition, the death rate was 16.7 per cent for white patients, against 28.6 per cent for the colored. Because of the peculiar fact, for which I am not prepared to offer an explanation, that the class of patients admitted varied considerably for the two races, the death rate for all cases is higher for white obstetrical cases (1.9 per cent) than for the colored (1.5 per cent). This difference provides an excellent illustration of statistical fallacies, when conclusions are arrived at upon the basis of *mere* numbers, without reference to the constituent units, which should always be taken into account and subjected to critical analysis. If the number of white obstetrical cases admitted had been distributed according to the condition on admission, in the same manner as the colored, the corrected white death rate would have been 1.4 per cent, instead of 1.9 per cent, as actually shown, according to the tables. If the colored admissions had been distributed in the same manner as the white patients, the corrected colored death rate would have been 2.0 per cent, instead of 1.5 per cent, as shown, according to the tables. In part, this curious result is due to the fact that the proportion of cases of operative labor was 15.4 per cent of the total for white patients, against 12.1 per cent for the colored. Since the death rate in this group is considerably above the average, the rate for all cases is materially increased by this larger proportion. The same is true of cases of abortion, which, for white patients, formed 10.8 per cent of the total, against only 6.2 per cent for the colored. The death rate in this group was 4.7 per cent for the white patients, against only 1.1 per cent for the colored. The tables are an interesting contribution to obstetrical knowledge and are deserving of careful study, with the suggestion of a more extended inquiry into the mortality in pregnancy according to race.

Some Anomalies in Hospital Experience.—There are many other interesting anomalies in the actual and relative admissions for specified causes, according to sex and race, but since all of the facts are given in detail in the alphabetical tables, they need only be very briefly referred to. Perhaps the most interesting disclosure of the analysis is the much higher proportion of male admissions for pernicious anæmia, amœbic dysentery, catarrhal jaundice, malarial fever, and other diseases probably of tropical or subtropical origin. These admissions are of more than local significance, since it is practically certain that many Americans returning from the Panama Canal Zone, Porto Rico, Cuba, etc., are materially impaired in health on account of tropical residence. Another suggestive contrast in the number of admissions is found in exophthalmic goiter, although it is well known that this affliction is more common among women than men.* Finally, attention may be drawn to the fact that there were 37 admissions on account of lead-poisoning for white males, against only one such admission for white females. A further analysis by occupations could possibly be made, which would add to our information regarding the occurrence of industrial lead-poisoning in different sections of the country.

Dispensary Statistics.—The statistics of institutional morbidity, as thus far discussed, are more or less impaired in value by the fact that they do not include the entire hospital admissions of the city of Baltimore, and furthermore by the omission of dispensary cases, which, no doubt, include many patients more or less suitable for ward treatment. It has not been feasible to give extended consideration to the dispensary statistics, partly because the information is not given by race, which, as pointed out in the earlier discussion, is absolutely essential for a full understanding of the relative importance of particular facts. It has seemed, however, advisable to bring the available statistics together in a form convenient for future reference, and, accordingly, the facts are presented in Tables 62-70 of the Appendix. The tables differentiate the patients treated in the fourteen departments, excluding the statistics of the Roentgen-ray treatment, radiographs, and fluoroscopic examinations, which are given in detail in Table 71. It need only to be stated that the number of dispensary cases increased from 592,458, during the decade ending with 1901, to 720,674, during the decade ending with 1911, to emphasize the practical importance of a complete analysis of hospital statistics of this kind.

X-Ray Department Statistics.—With reference to the statistics of the X-Ray Department, it may be stated that during the period 1903-1911, 476 cases were treated, including 7,282 treatments, and 15,026 radiographs were made and 995 fluoroscopic examinations.

Financial Statistics.—It has also not been feasible to present an analysis of the financial statistics of The Johns Hopkins Hospital, which have only been given in detail in the report for 1912, but in an admirable manner, with the comparative data for the four previous years. These tables are self-explanatory and emphasize some of the more important facts of hospital experience from a financial point of view, it being shown, among other facts, that the average gross cost per patient per day increased from $2.88 in 1907 to $3.61 in 1911, and the net cost increased from $1.26 in 1907 to $1.69 in 1911. An excellent table contained in the 1912 report gives the expenses of the hospital, in detail, for all of the important items, and also for the five-year period 1907-1911. In course of time this information must become exceedingly valuable to the student of hospital economics, efficiency and methods of treatment, related to cost.*

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* The admission rate for white males being 0.3 per 10,000 of population as against 0.1 for colored males; and for white females 1.0 against 0.2 for the colored.

Average Number of Days of Treatment.—For the purpose of presenting in a convenient form the aggregate experience of The Johns Hopkins Hospital during the last twenty years, with reference to patients treated and the number of days of treatment, as well as the average for each year, I have abstracted the required information from the several annual reports, and the same are given in detail in Table 61 of the Statistical Appendix. According to this table, the average number of days of treatment decreased from 24.2 during the first decade to 22.1 during the last. The highest average occurred in 1892, or 27.4 days, and the lowest in 1911, or 19.3 days. Unfortunately, the number of days of treatment is not given by particular causes, which for medical, as well as for economic, purposes would be quite useful. It is well known, of course, that the average duration of sickness varies with the different causes of sickness, but concerning the exact duration there is as yet, at least for the United States, very little trustworthy information. To provide the data for an estimate as regards the economic cost of sickness, it is necessary that the duration of sickness, whether institutional or otherwise, as well as the approximate cost thereof, should be known. Given the average duration and the average cost per patient per day, it is feasible to calculate the economic cost of sickness due to particular causes with approximate accuracy, which is about all that is required to be shown.

Conclusions.—In concluding this analysis of The Johns Hopkins Hospital experience, I desire to express my profound appreciation of the person, unknown to me, who, with remarkable foresight, established the existing statistical basis for an intelligent presentation of the facts. I am not aware of any other hospital in the United States for which the required information is presented in an equally admirable manner, and out of the experience of which so much useful information can be drawn, not only for the benefit of the student of medicine and surgery, but also for students of economics and insurance. If the analysis, as here presented, facilitates the scientific study of medicine in its larger aspects as a community problem, I shall feel amply repaid for the labor necessary to present the facts in a more convenient form than in the annual reports, which must necessarily be accessible only to the few. Much, however, is gained by a consolidation of the facts for a period of sufficient length, and I feel that the combined data for the last decade meet all reasonable statistical, as well as medical, requirements. By presenting the experience of a large hospital, typical of modern methods of medical and surgical treatment, in a convenient form, a basis has been provided for a beginning, at least, in modern uniform hospital statistics, which are absolutely necessary as an aid towards the study of medical problems in their relation to broad questions of public policy. It is also to be hoped that as the result of this investigation The Johns Hopkins Hospital may be induced to adopt the Bellevue Hospital classification, as practically the most suitable for medical and other purposes. In return, the hope may be indulged that Bellevue Hospital, and other great hospitals throughout the country as well, may be induced to adopt, in their reports, the method of statistical presentation which has been successfully carried forward from year to year by The Johns Hopkins Hospital from its beginning, and which, if adopted by other institutions, would bring order out of chaos and make the enormous amount of hospital experience really useful to the student of medicine, as well as of many other branches of learning, vitally interested in the facts which have a much broader social and economic significance than is usually assumed to be the case.

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* See table 72 of the Statistical Appendix.

List of References to Address on the Statistical Experience Data of The Johns Hopkins Hospital, 1892-1911.

The Relation of the Hospital to Medical Education and Research, by William H. Welch, M. D., Journal of the American Medical Association, August 17, 1907.

Comparative Study of the Routine Treatment of Certain Diseases in Four of the Large New York Hospitals, by Henry P. Loomis, M. D., New York Medical Record, January 10, 1903.

A Bureau of Hospital Information, by M. E. McCalmont, The Dietetic & Hygienic Gazette.

Symposium on Hospital Statistics, etc., Journal of the American Medical Association, November, 1912.

Report on Death Certification, ordered to be printed by the House of Commons, August 15 and September 1, 1893, London, 1893.

A Plea for a More Liberal Nomenclature of the Naval Medical Service, Navy Medical Bulletin, January, 1912.

Nomenclature of Diseases Prepared for the Use of the Medical Officers of the United States Medical Hospital Service, Washington, 1874.

International Classification of Causes of Sickness and Death, published by the Division of Vital Statistics, Bureau of the Census, Washington, 1910.

Annual Reports of The Johns Hopkins Hospital, 1892-1911.

Tenth Annual Report Bellevue and Allied Hospitals, State of New York, 1912.

Discussion on Nosography, Transactions New York State Medical Association, 1888.

Practical Conditions Concerning the Human Nosography, by J. W. S. Gouley, Transactions of the International Medical Congress, Washington, 1887.

Address on Human Nosography, by J. W. S. Gouley, M. D., New York State Medical Association, 1887.

* The list of references includes quite a number of works not referred to in the text but made use of in the preparation of the paper, with particular reference to the importance of disease registration and the practical utility of institutional and other morbidity records as an aid towards the more successful solution of pressing problems of labor, social service, medicine, public health and insurance.

Nomenclature for the Different Classes of Infectious Diseases, by W. H. Thomson, Transactions New York Academy of Medicine, 1894.

Statistics of Health, by T. R. Edmonds, Report of the Proceedings of the Fourth Session of the International Statistical Congress, London, 1861.

Report on Nomenclature of Diseases, by Dr. Francis G. Smith, New York Medical Record, 1872.

The Budapest System of Death Classification, by Frederick L. Hoffman, American Journal of Public Hygiene, February, 1910.

Report of Committee on Classification of Diseases and Causes of Death, Proceedings American Association of Medical Examiners, June, 1909.

Report of Committee on Scientific Nomenclature, New York Medical Record, June 12, 1909.

Unsatisfactory Returns of Causes of Death, Monthly Bulletin of the State Board of Health of Michigan, December, 1908.

A Simple, Efficient, and Elastic System for Indexing Case Histories and Filing Current Literature and References, New York Medical Record, November 2, 1912.

Report of the Committee on Clinical Nomenclature, Vincent Y. Bowditch, Chairman (n. d.).

The Nomenclature and Classification of Diseases, by Surgeon-General George M. Sternberg, U. S. Army, March, 1895.

The Nomenclature of Diseases, Journal American Medical Association, August 8, 1896.

Report on the Registration of Prevalent Diseases, by T. W. Draper, M. D., Boston, 1876.

Systematic Study of the Causes of Sickness and Death, by H. B. Baker, M. D., Lansing, Mich., 1881.

Digest of the Laws and Regulations of the Various States Relating to the Reporting of Causes of Sickness, by John W. Trask, Government Printing Office, Washington, 1911.

Some of the Defects in the Present System of Registration of Deaths in England and Wales, by Arthur Ransome, Manchester, England, 1867.

Inquest Under National Authority, Senate Report, No. 517 Fiftieth Congress, First Session, March 12, 1888.

A Report on a Uniform System of Registration of Causes of Death Throughout the United States, by Charles P. Russell, M. D., New York.

New Tables issued by the Local Government Board and Schedule of Causes of Death, London, 1901.

Report on Uniform System of Births and Deaths Registrations, House of Representatives, Fifty-seventh Congress, First Session, Report No. 1932, May 7, 1902.

Relation of Physicians to Mortality Statistics, U. S. Census Office, Washington, 1903.

Manual of the International List of Causes of Death, Government Printing Office, Washington, D. C., 1911. Reprint 1913.

Defects in Registration, by F. D. Beagle, New York State Department of Health, Albany, 1908.

Report on Diseases in the Philadelphia Dispensary, The Philadelphia Medical Museum, Vol. I, Philadelphia, 1805.

Observations on the Statistics of Sickness, Insurance Monitor, New York, 1884.

A Study of Diseases, by Dr. R. S. Keelor, Proceedings National Association of Accident Underwriters, July 8, 1903.

Sickness Experience in Friendly Societies, British Medical Journal, August 13, 1910.

Statistics of Puerperal Fever and Allied Infectious Diseases, by George Geddes, Bristol, 1912.

Annual Reports of the Metropolitan Asylum Board, London.

The Hospital and the Community, Journal American Medical Association, June 13, 1908.

Essay and Paper on Some Fallacies of Statistics, by Henry W. Rumsey, M. D., London, 1875.

Manual on the International List of Causes of Death for Official Use, London, 1912.

The Nomenclature of Diseases drawn up by a Joint Committee appointed by the Royal College of Physicians of London, 3d edition, London, 1896; 4th edition, London, 1906.

The Bellevue Hospital Nomenclature of Diseases and Conditions, with Rules for the Recording and Filing of Returns, New York, 1911.

Nomenclature of Diseases and Injuries, adopted by the Medical Department of the U. S. Navy, Government Printing Office, Washington, 1912.

Wasted Records of Disease, by Charles E. Paget, published by Edward Arnold, London, 1897.

Statistics of Benevolent Institutions of the United States, The Survey, New York, February 15, 1913.

Special Report on Benevolent Institutions, by John Koren, Expert Special Agent, Bureau of the Census, Washington, 1905.

Proposals for an Uniform Plan of Hospital Statistics, Proceedings of the Fourth Session of the International Statistical Congress, held in London, July, 1860. Pub. London, 1861.

The Registration of Diseases, by William C. Rogers, M. D., Transactions of the Medical Society of the State of New York, Albany, 1859.

Statistics of Sickness Derived from Medical Experience, by Thomas C. Brumsmade, M. D., Transactions of the Medical Society of the State of New York, Albany, 1858.

Statistical Nosology, Transactions of the Medical Society of the State of New York, Albany, 1858.

Numerical Analysis of Patients Treated in Guy's Hospital, 1854-61, Journal of the Royal Statistical Society, Vol. XXIV, 1861.

Report on the Mortality of London Hospitals, Journal of the Royal Statistical Society, Vol. XXX, London, 1867.

The Importance of Collecting Hospital Records, by Robert D. Coughlin, New York Medical Record, Vol. IX, 1911.

The Mortality of Hospitals, General and Special, in the United Kingdom in Past and Present, Journal of the Royal Statistical Society, Vol. XL, London, 1877.

Report on the Hospitals of the United Kingdom, John S. Bristowe, M. D., and Timothy Holmes, Privy Council, Medical Report, London, 1863.

Sickness Statistics, by H. B. Baker, Lansing, Mich., 1892.

A National System of Notification and Registration of Sickness, by Arthur Newsholme, M. D., Jour. Royal Stat. Soc., March, 1896, Vol. LIX.

Sickness Statistics Report of the Committee on Vital Statistics of the National Conference of State Boards of Health, by Henry B. Baker, M. D., Lansing, Mich., 1892.

The Defects of Medical Terminology, British Medical Journal, September 21, 1912.

Air, Food and Exercise, by Rabaglati, New York, 1904. (Includes important discussion of terms, definitions, etc.)

Diseases of the House Officers in Hospitals, Journal American Medical Association, December 19, 1903.

Nosology of Diseases Arranged in their Classes, etc., by W. Cullen, London, 1808.

A Synopsis of Nosology, by W. Cullen, translated by Henry Wilkes, Philadelphia, 1793.

Dictionary of Medicine, by Gould and Pyle, Philadelphia, 1907.

Hospital Morbidity Statistics, by C. F. Bolduan, New York Medical Journal, March 29, 1913.

Morbidity and Morphology, by R. B. Bean, Johns Hopkins Hospital Bulletin, December, 1912.

The Surgical Peculiarities of the American Negro, by R. Matas, Transactions of the American Surgical Association, 1896.

Medical and Surgical History of the War of the Rebellion, by Surgeon-General J. K. Barnes, Washington, 1870.

Medical and Anthropological Statistics of the Provost-Marshal-General's Bureau of the War of the Rebellion, Washington, 1875.

Relation of Morbidity Reports to Public Health Administration, by J. W. Trask, M. D., American Journal of Public Health, Vol. III, No. 5, May, 1913.

Morbidity Reports, Their Purpose and Present Status, by John W. Trask, M. D., Journal of the American Medical Association, September 20, 1913.

Report of the Special Committee on Morbidity and Mortality Statistics in the United Kingdom, Journal of the Royal Statistical Society, July, 1913.

The Promotion of Uniformity in the Registration of Diseases in Hospitals, R. F. Tobin, Medical Press and Circular, Vol. LXXV, 1908.

Benevolent Hospitals in Metropolitan Boston; William H. Mahoney, Quar. Pubs. American Statistical Association, June, 1913.

Age Incidence, Sex, and Comparative Frequency in Disease, James G. Andrew, Glasgow, 1909.

Report of the Local Government Board on Statistics of the Incidence of Notifiable Infectious Diseases in Each Sanitary District in England and Wales. London, 1913.

Statistical Appendix to Address on the Statistical Experience Data of The Johns Hopkins Hospital, 1892-1911.

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MORTALITY AND MORBIDITY STATISTICS OF THE JOHNS HOPKINS HOSPITAL, 1892-1911.

TABLE 1. SUMMARY OF WHITE AND COLORED PATIENTS.

	Males.					Females.				
Year.	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	1155	813	70.4	94	8.1	1098	773	70.4	66	6.0
1893	1360	974	71.6	107	7.9	1262	843	66.8	59	4.7
1894	1528	1064	69.6	133	8.7	1490	1022	68.6	64	4.3
1895	1821	1331	73.1	143	7.9	1565	1087	69.5	93	5.9
1896	1864	1331	71.4	128	6.9	1738	1206	69.4	87	5.0
1897	1818	1308	71.9	132	7.3	1815	1313	72.3	85	4.7
1898	1930	1475	76.4	137	7.1	1885	1405	74.5	102	5.4
1899	2099	1546	73.7	160	7.6	1975	1456	73.7	94	4.8
1900	2396	1733	72.3	179	7.5	2306	1641	71.2	129	5.6
1901	2236	1603	71.7	199	8.9	2127	1584	74.5	96	4.5
1902	2028	1439	71.0	181	8.9	2136	1553	72.7	123	5.8
1903	2076	1528	73.6	168	8.1	2090	1536	73.5	94	4.5
1904	2296	1659	72.3	177	7.7	2235	1668	74.6	103	4.6
1905	2041	1482	72.6	153	7.5	2183	1668	76.4	90	4.1
1906	2154	1492	69.3	178	8.3	2396	1829	76.3	85	3.5
1907	2268	1581	69.7	176	7.8	2591	1962	75.7	95	3.7
1908	2313	1591	68.8	187	8.1	2599	2016	77.6	76	2.9
1909	2524	1757	69.6	175	6.9	2561	1970	76.9	111	4.3
1910	2595	1840	70.9	159	6.1	2672	2025	75.8	99	3.7
1911	2524	1725	68.3	190	7.5	2675	2033	76.0	103	3.9
1892-01..	18207	13178	72.4	1412	7.8	17261	12330	71.4	875	5.1
1902-11..	22819	16094	70.5	1744	7.6	24138	18260	75.6	979	4.1

SEC. A. WHITE PATIENTS, SEX AND AGE, 1892-1911.

Table 2. Summary of White Patients.

Year.	Males.					Females.				
	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	1006	723	71.9	73	7.3	958	690	72.0	46	4.8
1893	1185	852	71.9	83	7.0	1111	734	66.1	48	4.3
1894	1335	937	70.2	107	8.0	1289	902	70.0	44	3.4
1895	1553	1169	75.3	106	6.8	1341	943	70.3	66	4.9
1896	1578	1139	72.2	100	6.3	1452	1025	70.6	68	4.7
1897	1515	1100	72.6	90	5.9	1515	1113	73.5	61	4.0
1898	1566	1226	78.3	93	5.9	1491	1119	75.1	63	4.2
1899	1703	1260	74.0	115	6.8	1570	1159	73.8	59	3.8
1900	1923	1406	73.1	124	6.4	1796	1278	71.2	89	5.0
1901	1804	1300	72.1	137	7.6	1616	1212	75.0	58	3.6
1902	1653	1177	71.2	128	7.7	1633	1181	72.3	85	5.2
1903	1701	1256	73.8	123	7.2	1567	1141	72.8	60	3.8
1904	1857	1357	73.1	118	6.4	1625	1201	73.9	65	4.0
1905	1645	1209	73.5	97	5.9	1590	1204	75.7	63	4.0
1906	1741	1197	68.7	128	7.4	1714	1293	75.4	50	2.9
1907	1887	1314	69.6	128	6.8	1892	1424	75.3	60	3.2
1908	1919	1338	69.7	130	6.8	1921	1472	76.6	50	2.6
1909	2101	1443	68.7	127	6.0	1868	1431	76.6	76	4.1
1910	2144	1518	70.8	118	5.5	1959	1440	73.5	68	3.5
1911	2144	1473	68.7	138	6.4	1906	1428	74.9	60	3.1
1892-01..	15168	11112	73.3	1028	6.8	14139	10175	72.0	602	4.3
1902-11..	18792	13282	70.7	1235	6.6	17675	13215	74.8	637	3.6

Table 3. White Medical Cases.

Year.	Males.					Females.				
	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	546	374	68.5	53	9.7	226	154	68.1	18	8.0
1893	648	435	67.1	53	8.2	272	175	64.3	19	7.0
1894	636	431	67.8	73	11.5	292	199	68.2	18	6.2
1895	700	522	74.6	56	8.0	285	178	62.5	32	11.2
1896	777	552	71.0	70	9.0	328	214	65.2	23	7.0
1897	726	507	69.8	50	6.9	334	227	68.0	29	8.7
1898	733	569	77.6	48	6.5	312	222	71.2	21	6.7
1899	777	548	70.5	70	9.0	357	244	68.3	17	4.8
1900	890	617	69.3	75	8.4	447	298	66.7	38	8.5
1901	866	589	68.0	80	9.2	356	252	70.8	21	5.9
1902	737	522	70.8	61	8.3	339	218	64.3	33	9.7
1903	789	554	70.2	68	8.6	374	270	72.2	20	5.3
1904	790	544	68.9	64	8.1	347	240	69.2	26	7.5
1905	726	490	67.5	51	7.0	326	209	64.1	23	7.1
1906	771	481	62.4	67	8.7	420	279	66.4	18	4.3
1907	843	507	60.1	77	9.1	426	266	64.8	17	4.0
1908	832	539	64.8	62	7.5	453	294	64.9	18	4.0
1909	874	528	60.4	70	8.0	477	281	58.9	27	5.7
1910	914	583	63.8	49	5.4	530	320	60.4	24	4.5
1911	937	588	62.8	55	5.9	494	303	61.3	17	3.4
1892-01..	7299	5144	70.5	628	8.6	3209	2163	67.4	236	7.4
1902-11..	8213	5336	65.0	624	7.6	4186	2680	64.0	223	5.3

TABLE 4. WHITE SURGICAL CASES.

	Males.					Females.				
Year.	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	460	349	75.9	20	4.3	156	114	73.1	7	4.5
1893	537	417	77.7	30	5.6	203	145	71.4	10	4.9
1894	699	506	72.4	34	4.9	287	196	68.3	12	4.2
1895	853	647	75.8	50	5.9	308	238	77.3	8	2.6
1896	801	587	73.3	30	3.7	313	235	75.1	17	5.4
1897	789	593	75.2	40	5.1	297	222	74.7	18	6.1
1898	833	657	78.9	45	5.4	302	231	76.5	15	5.0
1899	926	712	76.9	45	4.9	306	224	73.2	16	5.2
1900	1033	789	76.4	49	4.7	359	243	67.7	24	6.7
1901	938	711	75.8	57	6.1	349	259	74.2	19	5.4
1902	916	655	71.5	67	7.3	345	246	71.3	16	4.6
1903	912	702	77.0	55	6.0	363	252	69.4	16	4.4
1904	1067	813	76.2	54	5.1	398	294	73.9	25	6.3
1905	919	719	78.2	46	5.0	355	271	76.3	20	5.6
1906	970	716	73.8	61	6.3	375	284	75.7	18	4.8
1907	1044	807	77.3	51	4.9	434	321	74.0	29	6.7
1908	1087	799	73.5	68	6.3	423	308	72.8	19	4.5
1909	1227	915	74.6	57	4.6	429	313	73.0	33	7.7
1910	1230	935	76.0	69	5.6	461	318	69.0	26	5.6
1911	1207	885	73.3	83	6.9	471	335	71.1	21	4.5
1892-01..	7869	5968	75.8	400	5.1	2880	2107	73.2	146	5.1
1902-11..	10579	7946	75.1	611	5.8	4054	2942	72.6	223	5.5

TABLE 5. WHITE GYNECOLOGICAL AND OBSTETRICAL CASES.

	Gynecological cases.					Obstetrical cases.				
Year	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	576	422	73.3	21	3.6	.....	.....	...	...	..
1893	636	414	65.1	19	3.0	.....	.....	...	...	..
1894	710	507	71.4	14	2.0	.....	.....	...	...	..
1895	748	527	70.5	26	3.5	.....	.....	...	...	..
1896	801	572	71.4	28	3.5	10	4	40.0	...	..
1897	785	585	74.5	13	1.7	99	79	79.8	1	1.0
1898	731	542	74.1	26	3.6	146	124	84.9	1	0.7
1899	771	583	75.6	23	3.0	136	108	79.4	3	2.2
1900	815	605	74.2	24	2.9	175	132	75.4	3	1.7
1901	775	597	77.0	17	2.2	136	104	76.5	1	0.7
1902	747	555	74.3	29	3.9	202	162	80.2	7	3.5
1903	674	491	72.8	22	3.3	156	128	82.1	2	1.3
1904	665	481	72.3	12	1.8	215	186	86.5	2	0.9
1905	662	509	76.9	12	1.8	247	215	87.0	8	3.2
1906	673	523	77.7	11	1.6	246	207	84.1	3	1.2
1907	755	585	77.5	11	1.5	277	252	91.0	3	1.1
1908	719	586	81.5	9	1.3	326	284	87.1	4	1.2
1909	642	545	84.9	8	1.2	320	292	91.3	8	2.5
1910	671	536	79.9	13	1.9	297	266	89.6	5	1.7
1911	595	489	82.2	14	2.4	346	301	87.0	8	2.3
1892-01..	7348	5354	72.9	211	2.9	702	551	78.5	9	1.3
1902-11..	6803	5300	77.9	141	2.1	2632	2293	87.1	50	1.9

Table 6. White Patients, Ages Under 15.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	106	4	3.8	52	2	3.8
1893	105	4	3.8	70	5	7.1
1894	137	6	4.4	112	5	4.5
1895	199	6	3.0	120	9	7.5
1896	222	6	2.7	174	7	4.0
1897	203	11	5.4	165	6	3.6
1898	204	7	3.4	184	8	4.3
1899	159	8	5.0	90	5	5.6
1900	223	11	4.9	130	9	6.9
1901	170	9	5.3	109	7	6.4
1902	179	20	11.1	95	9	9.5
1903	206	17	8.3	116	5	4.3
1904	193	15	7.8	106	12	11.3
1905	159	9	5.7	111	14	12.6
1906	172	16	9.3	131	6	4.6
1907	234	27	11.5	128	14	10.9
1908	260	24	9.2	129	12	9.3
1909	263	22	8.4	137	22	16.1
1910	228	18	7.9	153	12	7.8
1911	261	22	8.4	146	11	7.5
1892-01....	1728	72	4.2	1206	63	5.2
1902-11....	2155	190	8.9	1252	117	9.3

Table 7. White Patients, Ages 15-24.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	231	14	6.1	209	7	3.3
1893	245	8	3.3	272	10	3.7
1894	308	8	2.6	314	7	2.2
1895	363	8	2.2	330	13	3.9
1896	364	12	3.3	353	16	4.5
1897	357	22	6.2	377	19	5.0
1898	363	28	7.7	404	16	4.0
1899	308	13	4.2	345	6	1.7
1900	314	18	5.7	418	13	3.1
1901	349	12	3.4	348	7	2.0
1902	313	13	4.2	354	19	5.4
1903	332	11	3.3	354	9	2.5
1904	369	11	3.0	406	8	2.0
1905	299	6	2.0	418	6	1.4
1906	356	14	3.9	549	8	1.5
1907	416	12	2.9	550	10	1.8
1908	374	16	4.3	599	6	1.0
1909	409	14	3.4	533	10	1.9
1910	398	12	3.0	558	13	2.3
1911	425	19	4.5	567	8	1.4
1892-01....	3202	143	4.5	3370	114	3.4
1902-11....	3691	128	3.5	4888	97	2.0

TABLE 8. WHITE PATIENTS, AGES 25-34.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	196	19	9.7	293	9	3.1
1893	270	14	5.2	360	2	0.6
1894	324	11	3.4	359	4	1.1
1895	405	12	3.0	370	6	1.6
1896	401	15	3.7	383	12	3.1
1897	398	35	8.8	435	25	5.7
1898	415	42	10.1	400	31	7.8
1899	367	22	6.0	463	16	3.5
1900	451	25	5.5	549	12	2.2
1901	408	21	5.1	476	4	0.8
1902	352	11	3.1	508	14	2.8
1903	360	17	4.7	466	13	2.8
1904	409	20	4.9	466	8	1.7
1905	357	12	3.4	473	10	2.1
1906	363	17	4.7	450	9	2.0
1907	383	22	5.7	552	8	1.4
1908	359	21	5.8	523	13	2.5
1909	408	21	5.1	554	7	1.3
1910	393	14	3.6	518	8	1.5
1911	417	19	4.6	549	17	3.1
1892-01....	3635	216	5.9	4088	121	3.0
1902-11....	3801	174	4.6	5059	107	2.1

TABLE 9. WHITE PATIENTS, AGES 35-44.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	168	13	7.7	195	14	7.2
1893	223	21	9.4	193	9	4.7
1894	176	28	15.9	175	12	6.9
1895	201	33	16.4	185	15	8.1
1896	200	25	12.5	181	9	4.9
1897	212	12	5.7	196	5	2.6
1898	228	9	3.9	199	3	1.5
1899	338	25	7.4	343	12	3.5
1900	379	32	8.4	336	19	5.7
1901	347	26	7.5	359	16	4.5
1902	284	23	8.1	378	19	5.0
1903	291	27	9.3	339	15	4.4
1904	305	19	6.2	337	7	2.1
1905	284	15	5.3	322	13	4.0
1906	336	22	6.5	333	12	3.6
1907	313	20	6.4	356	13	3.7
1908	310	21	6.8	368	8	2.2
1909	355	15	4.2	329	16	4.9
1910	384	21	5.5	361	11	3.0
1911	342	21	6.1	359	12	3.3
1892-01....	2472	224	9.1	2362	114	4.8
1902-11....	3204	204	6.4	3482	126	3.6

Table 10. White Patients, Ages 45-54.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	152	7	4.6	118	11	9.3
1893	181	25	13.8	128	16	12.5
1894	210	21	10.0	152	7	4.6
1895	207	15	7.2	145	13	9.0
1896	199	18	9.0	155	15	9.7
1897	178	4	2.2	161	...	..
1898	164	5	3.0	153	3	2.0
1899	232	21	9.1	190	12	6.3
1900	274	22	8.0	204	17	8.3
1901	258	29	11.2	167	11	6.6
1902	249	23	9.2	167	14	8.4
1903	229	15	6.6	168	9	5.4
1904	273	27	9.9	168	13	7.7
1905	242	22	9.1	146	8	5.5
1906	224	24	10.7	165	9	5.5
1907	247	23	9.3	196	9	4.6
1908	272	14	5.1	197	8	4.1
1909	321	28	8.7	181	13	7.2
1910	292	15	5.1	236	14	5.9
1911	291	20	6.9	186	3	1.6
1892-01....	2055	167	8.1	1573	105	6.7
1902-11....	2640	211	8.0	1810	100	5.5

Table 11. White Patients, Ages 55-64.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	100	7	7.0	70	2	2.9
1893	117	4	3.4	71	4	5.6
1894	126	17	13.5	142	6	4.2
1895	126	20	15.9	154	4	2.6
1896	135	18	13.3	158	6	3.8
1897	123	5	4.1	136	5	3.7
1898	129	1	0.8	118	1	0.8
1899	185	14	7.6	103	5	4.9
1900	174	10	5.7	121	15	12.4
1901	180	25	13.9	114	10	8.8
1902	180	22	12.2	99	10	10.1
1903	176	18	10.2	92	8	8.7
1904	160	12	7.5	103	10	9.7
1905	190	19	10.0	86	9	10.5
1906	173	19	11.0	59	3	5.1
1907	194	18	9.3	86	4	4.7
1908	205	20	9.8	75	3	4.0
1909	215	13	6.0	93	2	2.2
1910	261	25	9.6	108	8	7.4
1911	242	19	7.9	75	7	9.3
1892-01....	1395	121	8.7	1187	58	4.9
1902-11....	1996	185	9.3	876	64	7.3

TABLE 12. WHITE PATIENTS, AGES 65 AND OVER.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	53	9	17.0	21	1	4.8
1893	44	7	15.9	17	2	11.8
1894	54	16	29.6	35	3	8.6
1895	52	12	23.1	37	6	16.2
1896	57	6	10.5	48	3	6.3
1897	44	1	2.3	45	1	2.2
1898	63	1	1.6	33	1	3.0
1899	114	12	10.5	36	3	8.3
1900	108	6	5.6	38	4	10.5
1901	92	15	16.3	43	3	7.0
1902	96	16	16.7	32	...	..
1903	107	18	16.8	32	1	3.1
1904	148	14	9.5	39	7	17.9
1905	114	14	12.3	34	3	8.8
1906	117	16	13.7	27	3	11.1
1907	100	6	6.0	24	2	8.3
1908	139	14	10.0	30	...	..
1909	130	14	10.8	41	6	14.6
1910	188	13	6.9	25	2	8.0
1911	166	18	10.8	24	2	8.3
1892-01....	681	85	12.5	353	27	7.6
1902-11....	1305	143	11.0	308	26	8.4

SEC. B. COLORED PATIENTS, SEX AND AGE, 1892-1911.

TABLE 13. SUMMARY OF COLORED PATIENTS.

	Males.					Females.				
Year.	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	149	90	60.4	21	14.1	140	83	59.3	20	14.3
1893	175	122	69.7	24	13.7	151	109	72.2	11	7.3
1894	193	127	65.8	26	13.5	201	120	59.7	20	10.0
1895	268	162	60.4	37	13.8	224	144	64.3	27	12.1
1896	286	192	67.1	28	9.8	286	181	63.3	19	6.6
1897	303	208	68.6	42	13.9	300	200	66.7	24	8.0
1898	364	249	68.4	44	12.1	394	286	72.6	39	9.9
1899	396	286	72.2	45	11.4	405	297	73.3	35	8.6
1900	473	327	69.1	55	11.6	510	363	71.2	40	7.8
1901	432	303	70.1	62	14.4	511	372	72.8	38	7.4
1902	375	262	69.9	53	14.1	503	372	74.0	38	7.6
1903	375	272	72.5	45	12.0	523	395	75.5	34	6.5
1904	439	302	68.8	59	13.4	610	467	76.6	38	6.2
1905	396	273	68.9	56	14.1	593	464	78.2	27	4.6
1906	413	295	71.4	50	12.1	682	536	78.6	35	5.1
1907	381	267	70.1	48	12.6	699	538	77.0	35	5.0
1908	394	253	64.2	57	14.5	678	544	80.2	26	3.8
1909	423	314	74.2	48	11.3	693	539	77.8	35	5.1
1910	451	322	71.4	41	9.1	713	585	82.0	31	4.3
1911	380	252	66.3	52	13.7	769	605	78.7	43	5.6
1892-01..	3039	2066	68.0	384	12.6	3122	2155	69.0	273	8.7
1902-11..	4027	2812	69.8	509	12.6	6463	5045	78.1	342	5.3

TABLE 14. COLORED MEDICAL CASES.

	Males.					Females.				
Year.	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	84	45	53.6	17	20.2	39	18	46.2	10	25.6
1893	98	64	65.3	17	17.3	35	21	60.0	9	25.7
1894	106	70	66.0	20	18.9	50	25	50.0	9	18.0
1895	128	71	55.5	33	25.8	62	35	56.5	13	21.0
1896	163	103	63.2	24	14.7	80	43	53.8	13	16.3
1897	164	101	61.6	33	20.1	66	37	56.1	13	19.7
1898	198	129	65.2	34	17.2	96	62	64.6	21	21.9
1899	211	146	69.2	34	16.1	92	62	67.4	20	21.7
1900	263	168	63.9	41	15.6	124	68	54.8	26	21.0
1901	263	182	69.2	42	16.0	113	71	62.8	18	15.9
1902	209	148	70.8	35	16.7	115	73	63.5	23	20.0
1903	221	160	72.4	32	14.5	91	65	71.4	15	16.5
1904	231	149	64.5	44	19.0	94	54	57.4	19	20.2
1905	194	120	61.9	35	18.0	94	60	63.8	12	12.8
1906	214	139	65.0	31	14.5	107	68	63.6	12	11.2
1907	193	119	61.7	35	18.1	103	55	53.4	21	20.4
1908	207	121	58.5	41	19.8	111	69	62.2	14	12.6
1909	219	149	68.0	31	14.2	119	71	59.7	19	16.0
1910	231	159	68.8	27	11.7	102	70	68.6	12	11.8
1911	190	123	64.7	31	16.3	110	65	59.1	19	17.3
1892-01..	1678	1079	64.3	295	17.6	757	442	58.3	152	20.1
1902-11..	2109	1387	65.8	342	16.2	1046	650	62.1	166	15.9

TABLE 15. COLORED SURGICAL CASES.

	Males.					Females.				
Year.	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	65	45	69.2	4	6.2	24	16	66.7	5	20.8
1893	77	58	75.3	7	9.1	33	28	84.8	1	3.0
1894	87	57	65.5	6	6.9	54	28	51.9	4	7.4
1895	140	91	65.0	4	2.9	52	37	71.2	2	3.8
1896	123	89	72.4	4	3.3	62	37	59.7	4	6.5
1897	139	107	77.0	9	6.5	53	38	71.7	3	5.7
1898	166	120	72.3	10	6.0	75	57	76.0	7	9.3
1899	185	140	75.7	11	5.9	65	41	63.1	8	12.3
1900	210	159	75.7	14	6.7	95	65	68.4	4	4.2
1901	169	121	71.6	20	11.8	83	62	74.6	8	9.6
1902	166	114	68.7	18	10.8	59	42	71.2	4	6.8
1903	154	112	72.7	13	8.4	81	59	72.8	7	8.6
1904	208	153	73.6	15	7.2	112	81	72.3	10	8.9
1905	202	153	75.7	21	10.4	95	73	76.8	5	5.3
1906	199	156	78.4	19	9.5	117	88	75.2	13	11.1
1907	188	148	78.7	13	6.9	116	88	75.9	7	6.0
1908	187	132	70.6	16	8.6	120	91	75.8	5	4.2
1909	204	165	80.9	17	8.3	95	65	68.4	6	6.3
1910	220	163	74.1	14	6.4	119	87	73.1	11	9.2
1911	190	129	67.9	21	11.1	159	122	76.7	11	6.9
1892-01..	1361	987	72.5	89	6.5	596	409	68.6	46	7.7
1902-11..	1918	1425	74.3	167	8.7	1073	796	74.2	79	7.4

TABLE 16. COLORED GYNECOLOGICAL AND OBSTETRICAL CASES.

Year.	Gynecological cases.					Obstetrical cases.				
	Treated.	Improved.	Per cent.	Died.	Per cent.	Treated.	Improved.	Per cent.	Died.	Per cent.
1892	77	49	63.6	5	6.5	.....	.....	...	...	..
1893	83	60	72.3	1	1.2	.....	.....	...	...	..
1894	97	67	69.1	7	7.2	.....	.....	...	...	..
1895	110	72	65.5	12	10.9	.....	.....	...	...	..
1896	128	90	70.3	2	1.6	16	11	68.8	...	..
1897	130	81	62.3	8	6.2	51	44	86.3	...	..
1898	145	101	69.7	9	6.2	78	66	84.6	2	2.6
1899	155	114	73.5	7	4.5	93	80	86.0	...	..
1900	176	134	76.1	7	4.0	115	96	83.5	3	2.6
1901	163	118	72.4	8	4.9	152	121	79.6	4	2.6
1902	171	123	71.9	7	4.1	158	134	84.8	4	2.5
1903	187	131	70.1	10	5.3	164	140	85.4	2	1.2
1904	210	160	76.2	5	2.4	194	172	88.7	4	2.1
1905	211	162	76.8	7	3.3	193	169	87.6	3	1.6
1906	274	223	81.4	5	1.8	184	157	85.3	5	2.7
1907	292	229	78.4	5	1.7	188	166	88.3	2	1.1
1908	263	217	82.5	5	1.9	184	167	90.8	2	1.1
1909	293	241	82.3	6	2.0	186	162	87.1	4	2.2
1910	308	260	84.4	8	2.6	184	168	91.3	...	..
1911	295	244	82.7	11	3.7	205	174	84.9	2	1.0
1892-01..	1264	886	70.1	66	5.2	505	418	82.8	9	1.8
1902-11..	2504	1990	79.5	69	2.8	1840	1609	87.4	28	1.5

TABLE 17. COLORED PATIENTS, AGES UNDER 15.

Year.	Males.			Females.		
	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	16	1	6.3	8	1	12.5
1893	14	...	...	6	1	16.7
1894	20	1	5.0	20	2	10.0
1895	36	4	11.1	24	2	8.3
1896	39	2	5.1	47	4	8.5
1897	33	6	18.2	39	6	15.4
1898	34	5	14.7	47	6	12.8
1899	57	4	7.0	27	2	7.4
1900	50	6	12.0	43	3	7.0
1901	36	6	16.7	50	6	12.0
1902	30	1	3.3	49	5	10.2
1903	40	6	15.0	47	6	12.8
1904	42	1	2.4	53	11	20.8
1905	52	6	11.5	48	8	16.7
1906	48	7	14.6	53	6	11.3
1907	51	6	11.8	68	1	1.5
1908	63	10	15.9	59	6	10.2
1909	46	6	13.0	63	8	12.7
1910	68	5	7.4	58	7	12.1
1911	53	6	11.3	95	11	11.6
1892-01....	335	35	10.4	311	33	10.6
1902-11....	493	54	11.0	593	69	11.6

TABLE 18. COLORED PATIENTS, AGES 15-24.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	45	6	13.3	48	7	14.6
1893	31	4	12.9	46	2	4.3
1894	29	5	17.2	37	3	8.1
1895	50	10	20.0	39	6	15.4
1896	55	4	7.3	55	6	10.9
1897	75	12	16.0	72	8	11.1
1898	96	13	13.5	97	12	12.4
1899	131	9	6.9	174	8	4.6
1900	136	9	6.6	197	7	3.6
1901	86	9	10.5	203	4	2.0
1902	98	8	8.2	215	7	3.3
1903	98	13	13.3	229	5	2.2
1904	115	12	10.4	284	7	2.5
1905	84	9	10.7	290	5	1.7
1906	113	12	10.6	324	7	2.2
1907	103	12	11.7	317	10	3.2
1908	91	11	12.1	323	7	2.2
1909	111	13	11.7	299	8	2.7
1910	116	8	6.9	319	4	1.3
1911	74	5	6.8	353	11	3.1
1892-01....	734	81	11.0	968	63	6.5
1902-11....	1003	103	10.3	2953	71	2.4

TABLE 19. COLORED PATIENTS, AGES 25-34.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	44	6	13.6	32	1	3.1
1893	46	3	6.5	51	3	5.9
1894	47	3	6.4	49	4	8.2
1895	62	9	14.5	58	7	12.1
1896	63	5	7.9	59	6	10.2
1897	73	12	16.4	62	4	6.5
1898	89	13	14.6	106	12	11.3
1899	90	4	4.4	77	5	6.5
1900	102	10	9.8	119	8	6.7
1901	102	10	9.8	128	10	7.8
1902	86	8	9.3	134	10	7.5
1903	79	10	12.7	137	5	3.6
1904	90	10	11.1	155	4	2.6
1905	94	14	14.9	138	3	2.2
1906	94	10	10.6	172	9	5.2
1907	84	10	11.9	167	7	4.2
1908	84	10	11.9	155	3	1.9
1909	87	7	8.0	196	7	3.6
1910	81	9	11.1	192	9	4.7
1911	80	13	16.3	183	5	2.7
1892-01....	718	75	10.4	741	60	8.1
1902-11....	859	101	11.8	1629	62	3.8

TABLE 20. COLORED PATIENTS, AGES 35-44.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	23	3	13.0	24	6	25.0
1893	32	4	12.5	27	3	11.1
1894	37	9	24.3	37	6	16.2
1895	45	10	22.2	40	9	22.5
1896	49	7	14.3	49	2	4.1
1897	51	8	15.7	55	2	3.6
1898	59	5	8.5	62	4	6.5
1899	62	5	8.1	46	6	13.0
1900	87	13	14.9	83	3	3.6
1901	89	15	16.9	83	10	12.0
1902	66	8	12.1	65	7	10.8
1903	65	6	9.2	64	7	10.9
1904	76	13	17.1	71	10	14.1
1905	65	13	20.0	75	5	6.7
1906	78	11	14.1	83	7	8.4
1907	70	10	14.3	81	8	9.9
1908	50	7	14.0	87	6	6.9
1909	80	9	11.3	87	5	5.7
1910	90	8	8.9	85	5	5.9
1911	67	12	17.9	88	8	9.1
1892-01....	534	79	14.8	506	51	10.1
1902-11....	707	97	13.7	786	68	8.7

TABLE 21. COLORED PATIENTS, AGES 45-54.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	8	3	37.5	18	2	11.1
1893	20	7	35.0	11	1	9.1
1894	23	2	8.7	20	4	20.0
1895	26	2	7.7	25	3	12.0
1896	24	10	41.7	30	1	3.3
1897	32	3	9.4	32	1	3.1
1898	32	5	15.6	43	2	4.7
1899	29	11	37.9	44	4	9.1
1900	57	6	10.5	40	9	22.5
1901	60	11	18.3	32	3	9.4
1902	67	19	28.4	27	4	14.8
1903	53	6	11.3	37	9	24.3
1904	64	16	25.0	28	4	14.3
1905	51	5	9.8	29	3	10.3
1906	37	9	24.3	33	3	9.1
1907	41	7	17.1	46	7	15.2
1908	57	9	15.8	42	3	7.1
1909	50	6	12.0	33	5	15.2
1910	56	7	12.5	37	3	8.1
1911	57	4	7.0	35	6	17.1
1892-01....	311	60	19.3	295	30	10.2
1902-11....	533	88	16.5	347	47	13.5

Table 22. Colored Patients, Ages 55-64.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	10	1	10.0	7	3	42.9
1893	27	5	18.5	5	1	20.0
1894	31	6	19.4	30	...	...
1895	36	1	2.8	28	...	...
1896	40	...	...	30	...	...
1897	26	...	...	26	3	11.5
1898	39	1	2.6	30	2	6.7
1899	14	7	50.0	18	4	22.2
1900	25	5	20.0	21	8	38.1
1901	45	9	20.0	9	3	33.3
1902	23	7	30.4	10	3	30.0
1903	29	4	13.8	5	1	20.0
1904	34	2	5.9	14	2	14.3
1905	33	7	21.2	8	2	25.0
1906	27	1	3.7	14	2	14.3
1907	22	1	4.5	19	2	10.5
1908	37	5	13.5	8	1	12.5
1909	33	5	15.2	14	2	14.3
1910	29	4	13.8	18	1	5.6
1911	32	8	25.0	15	2	13.3
1892-01....	293	35	11.9	204	24	11.8
1902-11....	299	44	14.7	125	18	14.4

Table 23. Colored Patients, Ages 65 and Over.

	Males.			Females.		
Year.	Treated.	Died.	Per cent.	Treated.	Died.	Per cent.
1892	3	1	33.3	3	...	...
1893	5	1	20.0	5	...	...
1894	6	...	...	8	1	12.5
1895	13	1	7.7	10	...	...
1896	16	...	...	16	...	...
1897	13	1	7.7	14	...	...
1898	15	2	13.3	9	1	11.1
1899	13	5	38.5	19	6	31.6
1900	16	6	37.5	7	2	28.6
1901	14	2	14.3	6	2	33.3
1902	5	2	40.0	3	2	66.7
1903	11	...	...	4	1	25.0
1904	18	5	27.8	5	...	...
1905	17	2	11.8	5	1	20.0
1906	16	...	...	3	1	33.3
1907	10	2	20.0	1	...	...
1908	12	5	41.7	4	...	...
1909	16	2	12.5	1	...	...
1910	11	...	...	4	2	50.0
1911	17	4	23.5	...	...	...
1892-01....	114	19	16.7	97	12	12.4
1902-11....	133	22	16.5	30	7	23.3

SEC. C. COMPARATIVE ADMISSION RATE, 1902-1911.

TABLE 24. SUMMARY OF WHITE CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	111	0.50	62	0.26
Blood	185	0.83	75	0.32
Bones and cartilages	389	1.75	140	0.59
Bursæ	27	0.12	12	0.05
Circulatory system	1171	5.28	315	1.33
Digestive system	2546	11.48	1711	7.23
Ductless glands and spleen	118	0.53	394	1.67
Ear	82	0.37	56	0.24
Eye and adnexa	182	0.82	79	0.33
Herniæ	903	4.07	229	0.97
Infective diseases	2843	12.82	1262	5.34
Joints	386	1.74	265	1.12
Lymphatic system	101	0.46	43	0.18
Mind	292	1.32	274	1.16
Miscellaneous	770	3.47	834	3.53
Muscles, fasciæ, tendons	102	0.46	48	0.20
Nervous system	1518	6.84	1195	5.05
Parasites	38	0.17	8	0.03
Poisonings, intoxications	137	0.62	40	0.17
Reproductive organs	1099	4.95	3472	14.68
Respiratory system	840	3.79	291	1.23
Skin, hair, nails	75	0.34	41	0.17
Tumors	1496	6.74	1731	7.32
Urinary organs	881	3.97	757	3.20
Obstetrical conditions	.....	....	2973	12.57
Newborn child	2	0.01	.....	....
Injuries	1436	6.47	350	1.48
Grand total	17730	79.93	16657	70.43

TABLE 25. SUMMARY OF COLORED CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10.000 population.
Abnormities, congenital malformations	11	0.29	14	0.31
Blood	10	0.27	13	0.29
Bones and cartilages	78	2.07	40	0.89
Bursæ	3	0.08	3	0.07
Circulatory system	581	15.43	165	3.65
Digestive system	387	10.28	441	9.76
Ductless glands and spleen	3	0.08	19	0.42
Ear	11	0.29	10	0.22
Eye and adnexa	25	0.66	29	0.64
Herniæ	131	3.48	56	1.24
Infective diseases	997	26.48	598	13.24
Joints	70	1.86	61	1.35
Lymphatic system	32	0.85	30	0.66
Mind	13	0.35	11	0.24
Miscellaneous	65	1.73	186	4.12
Muscles, fasciæ, tendons	12	0.32	6	0.13
Nervous system	112	2.97	94	2.08
Parasites	7	0.19	3	0.07
Poisonings, intoxications	8	0.21	6	0.13
Reproductive organs	81	2.15	1284	28.43
Respiratory system	391	10.38	137	3.03
Skin, hair, nails	51	1.35	45	1.00
Tumors	170	4.51	748	16.56
Urinary organs	200	5.31	140	3.10
Obstetrical conditions	.....	....	1868	41.35
Newborn child	1	0.03	.....	....
Injuries	312	8.29	107	2.37
Grand total	3762	99.90	6114	135.36

TABLE 26. WHITE MEDICAL CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	13	0.06	6	0.03
Blood	177	0.80	68	0.29
Bones and cartilages	26	0.12	9	0.04
Bursæ	2	0.01	2	0.01
Circulatory system	1044	4.71	273	1.15
Digestive system	760	3.43	421	1.78
Ductless glands and spleen	45	0.20	131	0.55
Ear	15	0.07	6	0.03
Eye and adnexa	8	0.04	11	0.05
Herniæ	6	0.03	.....	....
Infective diseases	2035	9.17	795	3.36
Joints	186	0.84	131	0.55
Lymphatic system	23	0.10	7	0.03
Mind	272	1.23	264	1.12
Miscellaneous	406	1.83	201	0.85
Muscles, fasciæ, tendons	26	0.12	12	0.05
Nervous system	1123	5.06	910	3.85
Parasites	7	0.03	6	0.03
Poisonings, intoxications	128	0.58	36	0.15
Reproductive organs	47	0.21	41	0.17
Respiratory system	657	2.96	222	0.94
Skin, hair, nails	32	0.14	25	0.11
Tumors	321	1.45	137	0.58
Urinary organs	392	1.77	182	0.77
Obstetrical conditions	.....	....	22	0.09
Newborn child	.....	....	.....	....
Injuries	19	0.09	7	0.03
Grand total	7770	35.03	3925	16.60

TABLE 27. WHITE SURGICAL CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	98	0.44	49	0.21
Blood	8	0.04	3	0.01
Bones and cartilages	363	1.64	124	0.52
Bursæ	25	0.11	10	0.04
Circulatory system	127	0.57	40	0.17
Digestive system	1786	8.05	866	3.66
Ductless glands and spleen	73	0.33	261	1.10
Ear	67	0.30	50	0.21
Eye and adnexa	174	0.78	68	0.29
Herniæ	897	4.04	127	0.54
Infective diseases	808	3.64	362	1.53
Joints	200	0.90	132	0.56
Lymphatic system	78	0.35	30	0.13
Mind	20	0.09	10	0.04
Miscellaneous	364	1.64	127	0.54
Muscles, fasciæ, tendons	76	0.34	36	0.15
Nervous system	395	1.78	250	1.06
Parasites	31	0.14	2	0.01
Poisonings, intoxications	9	0.04	1	....
Reproductive organs	1052	4.74	110	0.47
Respiratory system	183	0.83	68	0.29
Skin, hair, nails	43	0.19	13	0.05
Tumors	1175	5.30	703	2.97
Urinary organs	489	2.20	34	0.14
Obstetrical conditions	.....	....	4	0.02
Newborn child	2	0.01	.....	....
Injuries	1417	6.39	341	1.44
Grand total	9960	44.90	3821	16.16

TABLE 27A. WHITE GYNECOLOGICAL AND OBSTETRICAL CASES.

Diseases and conditions.	Gynecological cases.		Obstetrical cases.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	7	0.03	.....	....
Blood	4	0.02	.....	....
Bones and cartilages	7	0.03	.....	....
Bursæ	.....	....	.....	....
Circulatory system	2	0.01	.....	....
Digestive system	424	1.79	.....	....
Ductless glands and spleen	2	0.01	.....	....
Ear	.....	....	.....	....
Eye and adnexa	.....	....	.....	....
Herniæ	102	0.43	.....	....
Infective diseases	105	0.44	.....	....
Joints	2	0.01	.....	....
Lymphatic system	6	0.03	.....	....
Mind	.....	....	.....	....
Miscellaneous	506	2.14	.....	....
Muscles, fasciæ, tendons	.....	....	.....	....
Nervous system	35	0.15	.....	....
Parasites	.....	....	.....	....
Poisonings, intoxications	3	0.01	.....	....
Reproductive organs	3321	14.04	.....	....
Respiratory system	1	....	.....	....
Skin, hair, nails	3	0.01	.....	....
Tumors	891	3.77	.....	....
Urinary organs	541	2.29	.....	....
Obstetrical conditions	462	1.95	2485	10.51
Newborn child	.....	....	.....	....
Injuries	2	0.01	.....	....
Grand total	6426	27.17	2485	10.51

TABLE 28. COLORED MEDICAL CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	.....	....	.....	....
Blood	9	0.24	13	0.29
Bones and cartilages	3	0.08	1	0.02
Bursæ	1	0.03	.....	....
Circulatory system	549	14.58	153	3.39
Digestive system	102	2.71	62	1.37
Ductless glands and spleen	2	0.05	5	0.11
Ear	2	0.05	1	0.02
Eye and adnexa	3	0.08	4	0.09
Herniæ	.....	....	.....	....
Infective diseases	606	16.09	360	7.97
Joints	25	0.66	19	0.42
Lymphatic system	10	0.27	4	0.09
Mind	12	0.32	10	0.22
Miscellaneous	35	0.93	34	0.75
Muscles, fasciæ, tendons	7	0.19	1	0.02
Nervous system	71	1.89	65	1.44
Parasites	3	0.08	.....	....
Poisonings, intoxications	7	0.19	6	0.13
Reproductive organs	4	0.11	12	0.27
Respiratory system	368	9.77	125	2.77
Skin, hair, nails	3	0.08	4	0.09
Tumors	48	1.27	29	0.64
Urinary organs	115	3.05	70	1.55
Obstetrical conditions	.....	....	7	0.15
Newborn child	1	0.03	.....	....
Injuries	2	0.05	1	0.02
Grand total	1988	52.79	986	21.83

Table 29. Colored Surgical Cases.

Diseases and conditions.	Males.		Females.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	11	0.29	12	0.27
Blood	1	0.03	.....	....
Bones and cartilages	75	1.99	39	0.86
Bursæ	2	0.05	3	0.07
Circulatory system	32	0.85	12	0.27
Digestive system	285	7.57	207	4.58
Ductless glands and spleen	1	0.03	14	0.31
Ear	9	0.24	9	0.20
Eye and adnexa	22	0.58	25	0.55
Herniæ	131	3.48	33	0.73
Infective diseases	391	10.38	197	4.36
Joints	45	1.20	42	0.93
Lymphatic system	22	0.58	16	0.35
Mind	1	0.03	1	0.02
Miscellaneous	30	0.80	19	0.42
Muscles, fasciæ, tendons	5	0.13	5	0.11
Nervous system	41	1.09	26	0.58
Parasites	4	0.11	2	0.04
Poisonings, intoxications	1	0.03	.....	....
Reproductive organs	77	2.04	48	1.06
Respiratory system	23	0.61	11	0.24
Skin, hair, nails	48	1.27	39	0.86
Tumors	122	3.24	135	2.99
Urinary organs	85	2.26	9	0.20
Obstetrical conditions	.....	....	3	0.07
Newborn child	.....	....	.....	....
Injuries	310	8.23	106	2.35
Grand total	1774	47.11	1013	22.43

Table 29A. Colored Gynecological and Obstetrical Cases.

Diseases and conditions.	Gynecological cases.		Obstetrical cases.	
	Admitted.	Rate per 10,000 population.	Admitted.	Rate per 10,000 population.
Abnormities, congenital malformations	2	0.04	.....	....
Blood	.....	....	.....	....
Bones and cartilages	.....	....	.....	....
Bursæ	.....	....	.....	....
Circulatory system	.....	....	.....	....
Digestive system	172	3.81	.....	....
Ductless glands and spleen	.....	....	.....	....
Ear	.....	....	.....	....
Eye and adnexa	.....	....	.....	....
Herniæ	23	0.51	.....	....
Infective diseases	41	0.91	.....	....
Joints	.....	....	.....	....
Lymphatic system	10	0.22	.....	....
Mind	.....	....	.....	....
Miscellaneous	133	2.94	.....	....
Muscles, fasciæ, tendons	.....	....	.....	....
Nervous system	3	0.07	.....	....
Parasites	1	0.02	.....	....
Poisonings, intoxications	.....	....	.....	....
Reproductive organs	1224	27.10	.....	....
Respiratory system	1	0.02	.....	....
Skin, hair, nails	2	0.04	.....	....
Tumors	584	12.93	.....	....
Urinary organs	61	1.35	.....	....
Obstetrical conditions	131	2.90	1727	38.23
Newborn child	.....	....	.....	....
Injuries	.....	....	.....	....
Grand total	2388	52.87	1727	38.23

SEC. D. DISEASES AND CONDITIONS ON ADMISSION, 1902-1911.

TABLE 30. SUMMARY OF WHITE CASES.

	Males.		Females.	
Diseases and conditions.	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	111	0.6	62	0.4
Blood	185	1.0	75	0.5
Bones and cartilages	389	2.2	140	0.8
Bursæ	27	0.2	12	0.1
Circulatory system	1171	6.6	315	1.9
Digestive system	2546	14.4	1711	10.3
Ductless glands and spleen	118	0.7	394	2.4
Ear	82	0.5	56	0.3
Eye and adnexa	182	1.0	79	0.5
Herniæ	903	5.1	229	1.4
Infective diseases	2843	16.0	1262	7.6
Joints	386	2.2	265	1.6
Lymphatic system	101	0.6	43	0.3
Mind	292	1.6	274	1.6
Miscellaneous	770	4.3	834	5.0
Muscles, fasciæ, tendons	102	0.6	48	0.3
Nervous system	1518	8.6	1195	7.2
Parasites	38	0.2	8	...
Poisonings, intoxications	137	0.8	40	0.2
Reproductive organs	1099	6.2	3472	20.8
Respiratory system	840	4.7	291	1.7
Skin, hair, nails	75	0.4	41	0.2
Tumors	1496	8.4	1731	10.4
Urinary organs	881	5.0	757	4.5
Obstetrical conditions	.....	...	2973	17.8
Newborn child	2	...	.....	...
Injuries	1436	8.1	350	2.1
Grand total	17730	100.0	16657	100.0

TABLE 31. WHITE MEDICAL CASES.

	Males.		Females.	
Diseases and conditions.	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	13	0.2	6	0.2
Blood	177	2.3	68	1.7
Bones and cartilages	26	0.3	9	0.2
Bursæ	2	....	2	0.1
Circulatory system	1044	13.4	273	7.0
Digestive system	760	9.8	421	10.7
Ductless glands and spleen	45	0.6	131	3.3
Ear	15	0.2	6	0.2
Eye and adnexa	8	0.1	11	0.3
Herniæ	6	0.1	.....	....
Infective diseases	2035	26.2	795	20.3
Joints	186	2.4	131	3.3
Lymphatic system	23	0.3	7	0.2
Mind	272	3.5	264	6.7
Miscellaneous	406	5.2	201	5.1
Muscles, fasciæ, tendons	26	0.3	12	0.3
Nervous system	1123	14.5	910	23.2
Parasites	7	0.1	6	0.2
Poisonings, intoxications	128	1.6	36	0.9
Reproductive organs	47	0.6	41	1.0
Respiratory system	657	8.5	222	5.7
Skin, hair, nails	32	0.4	25	0.6
Tumors	321	4.1	137	3.5
Urinary organs	392	5.0	182	4.6
Obstetrical conditions	.....	....	22	0.6
Newborn child	.....	....	.....	....
Injuries	19	0.2	7	0.2
Grand total	7770	100.0	3925	100.0

TABLE 32. WHITE SURGICAL CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	98	1.0	49	1.3
Blood	8	0.1	3	0.1
Bones and cartilages	363	3.6	124	3.2
Bursæ	25	0.3	10	0.3
Circulatory system	127	1.3	40	1.0
Digestive system	1786	17.9	866	22.7
Ductless glands and spleen	73	0.7	261	6.8
Ear	67	0.7	50	1.3
Eye and adnexa	174	1.7	68	1.8
Herniæ	897	9.0	127	3.3
Infective diseases	808	8.1	362	9.5
Joints	200	2.0	132	3.5
Lymphatic system	78	0.8	30	0.8
Mind	20	0.2	10	0.3
Miscellaneous	364	3.7	127	3.3
Muscles, fasciæ, tendons	76	0.8	36	0.9
Nervous system	395	4.0	250	6.5
Parasites	31	0.3	2	0.1
Poisonings, intoxications	9	0.1	1	....
Reproductive organs	1052	10.6	110	2.9
Respiratory system	183	1.8	68	1.8
Skin, hair, nails	43	0.4	13	0.3
Tumors	1175	11.8	703	18.4
Urinary organs	489	4.9	34	0.9
Obstetrical conditions	.....	....	4	0.1
Newborn child	2	....	.....	....
Injuries	1417	14.2	341	8.9
Grand total	9960	100.0	3821	100.0

TABLE 33. WHITE GYNECOLOGICAL AND OBSTETRICAL CASES.

Diseases and conditions.	Gynecological cases.		Obstetrical cases.	
	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	7	0.1	.....	....
Blood	4	0.1	.....	....
Bones and cartilages	7	0.1	.....	....
Bursæ	.....	....	.....	....
Circulatory system	2	....	.....	....
Digestive system	424	6.6	.....	....
Ductless glands and spleen	2	....	.....	....
Ear	.....	....	.....	....
Eye and adnexa	.....	....	.....	....
Herniæ	102	1.6	.....	....
Infective diseases	105	1.6	.....	....
Joints	2	....	.....	....
Lymphatic system	6	0.1	.....	....
Mind	.....	....	.....	....
Miscellaneous	506	7.9	.....	....
Muscles, fasciæ, tendons	.....	....	.....	....
Nervous system	35	0.5	.....	....
Parasites	.....	....	.....	....
Poisonings, intoxications	3	0.1	.....	....
Reproductive organs	3321	51.7	.....	....
Respiratory system	1	....	.....	....
Skin, hair, nails	3	0.1	.....	....
Tumors	891	13.9	.....	....
Urinary organs	541	8.4	.....	....
Obstetrical conditions	462	7.2	2485	100.0
Newborn child	.....	....	.....	....
Injuries	2	....	.....	....
Grand total	6426	100.0	2485	100.0

TABLE 34. SUMMARY OF COLORED CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	11	0.3	14	0.2
Blood	10	0.3	13	0.2
Bones and cartilages	78	2.1	40	0.7
Bursæ	3	0.1	3	....
Circulatory system	581	15.4	165	2.7
Digestive system	387	10.3	441	7.2
Ductless glands and spleen	3	0.1	19	0.3
Ear	11	0.3	10	0.2
Eye and adnexa	25	0.7	29	0.5
Herniæ	131	3.5	56	0.9
Infective diseases	997	26.5	598	9.8
Joints	70	1.9	61	1.0
Lymphatic system	32	0.9	30	0.5
Mind	13	0.3	11	0.2
Miscellaneous	65	1.7	186	3.0
Muscles, fasciæ, tendons	12	0.3	6	0.1
Nervous system	112	3.0	94	1.5
Parasites	7	0.2	3	....
Poisonings, intoxications	8	0.2	6	0.1
Reproductive organs	81	2.2	1284	21.0
Respiratory system	391	10.4	137	2.2
Skin, hair, nails	51	1.4	45	0.7
Tumors	170	4.5	748	12.2
Urinary organs	200	5.3	140	2.3
Obstetrical conditions	.....	....	1868	30.6
Newborn child	1	....	.....	....
Injuries	312	8.3	107	1.8
Grand total	3762	100.0	6114	100.0

TABLE 35. COLORED MEDICAL CASES.

Diseases and conditions.	Males.		Females.	
	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	.....	....	.....	....
Blood	9	0.5	13	1.3
Bones and cartilages	3	0.2	1	0.1
Bursæ	1	0.1	.....	....
Circulatory system	549	27.6	153	15.5
Digestive system	102	5.1	62	6.3
Ductless glands and spleen	2	0.1	5	0.5
Ear	2	0.1	1	0.1
Eye and adnexa	3	0.2	4	0.4
Herniæ	.....	....	.....	....
Infective diseases	606	30.5	360	36.5
Joints	25	1.3	19	1.9
Lymphatic system	10	0.5	4	0.4
Mind	12	0.6	10	1.0
Miscellaneous	35	1.8	34	3.4
Muscles, fasciæ, tendons	7	0.4	1	0.1
Nervous system	71	3.6	65	6.6
Parasites	3	0.2	.....	....
Poisonings, intoxications	7	0.4	6	0.6
Reproductive organs	4	0.2	12	1.2
Respiratory system	368	18.5	125	12.7
Skin, hair, nails	3	0.2	4	0.4
Tumors	48	2.4	29	2.9
Urinary organs	115	5.8	70	7.1
Obstetrical conditions	.....	....	7	0.7
Newborn child	1	0.1	.....	....
Injuries	2	0.1	1	0.1
Grand total	1988	100.0	986	100.0

TABLE 36. COLORED SURGICAL CASES.

	Males.		Females.	
Diseases and conditions.	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	11	0.6	12	1.2
Blood	1	0.1	.....	....
Bones and cartilages	75	4.2	39	3.8
Bursæ	2	0.1	3	0.3
Circulatory system	32	1.8	12	1.2
Digestive system	285	16.1	207	20.4
Ductless glands and spleen	1	0.1	14	1.4
Ear	9	0.5	9	0.9
Eye and adnexa	22	1.2	25	2.5
Herniæ	131	7.4	33	3.3
Infective diseases	391	22.0	197	19.4
Joints	45	2.5	42	4.1
Lymphatic system	22	1.2	16	1.6
Mind	1	0.1	1	0.1
Miscellaneous	30	1.7	19	1.9
Muscles, fasciæ, tendons	5	0.3	5	0.5
Nervous system	41	2.3	26	2.6
Parasites	4	0.2	2	0.2
Poisonings, intoxications	1	0.1	.....	....
Reproductive organs	77	4.3	48	4.7
Respiratory system	23	1.3	11	1.1
Skin, hair, nails	48	2.7	39	3.8
Tumors	122	6.9	135	13.3
Urinary organs	85	4.8	9	0.9
Obstetrical conditions	.....	....	3	0.3
Newborn child	.....	....	.....	....
Injuries	310	17.5	106	10.5
Grand total	1774	100.0	1013	100.0

TABLE 37. COLORED GYNECOLOGICAL AND OBSTETRICAL CASES.

	Gynecological cases.		Obstetrical cases.	
Diseases and conditions.	Admitted.	Per cent.	Admitted.	Per cent.
Abnormities, congenital malformations	2	0.1	.....	....
Blood	.....	....	.....	....
Bones and cartilages	.....	....	.....	....
Bursæ	.....	....	.....	....
Circulatory system	.....	....	.....	....
Digestive system	172	7.2	.....	....
Ductless glands and spleen	.....	....	.....	....
Ear	.....	....	.....	....
Eye and adnexa	.....	....	.....	....
Herniæ	23	1.0	.....	....
Infective diseases	41	1.7	.....	....
Joints	.....	....	.....	....
Lymphatic system	10	0.4	.....	....
Mind	.....	....	.....	....
Miscellaneous	133	5.6	.....	....
Muscles, fasciæ, tendons	.....	....	.....	....
Nervous system	3	0.1	.....	....
Parasites	1	....	.....	....
Poisonings, intoxications	.....	....	.....	....
Reproductive organs	1224	51.3	.....	....
Respiratory system	1	....	.....	....
Skin, hair, nails	2	0.1	.....	....
Tumors	584	24.5	.....	....
Urinary organs	61	2.6	.....	....
Obstetrical conditions	131	5.5	1727	100.0
Newborn child	.....	....	.....	....
Injuries	.....	....	.....	....
Grand total	2388	100.0	1727	100.0

SEC. E. MORTALITY RATES BY CAUSES ON ADMISSION, WHITE PATIENTS, 1902-1911.

TABLE 38. SUMMARY OF WHITE CASES.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	111	5	4.5	62	3	4.8
Blood	185	42	22.7	75	13	17.3
Bones and cartilages	389	7	1.8	140	5	3.6
Bursæ	27	....	...	12	...	...
Circulatory system	1171	169	14.4	315	44	14.0
Arteries and veins	615	74	12.0	95	7	7.4
Endocardium and valves	397	71	17.9	180	29	16.1
Myocardium	120	16	13.3	27	6	22.2
Neuroses	24	2	8.3	5	...	...
Pericardium	15	6	40.0	8	2	25.0
Digestive system	2546	134	5.3	1711	58	3.4
Appendix	840	29	3.5	678	8	1.2
Intestine	252	28	11.1	168	17	10.1
Liver	189	29	15.3	36	5	13.9
Gall bladder and ducts	177	15	8.5	311	15	4.8
Mesentery	.....	....	...	.....	...	...
Omentum	.....	....	...	3	...	...
Peritoneum	30	10	33.3	56	7	12.5
Lips	3	....	...	.....	...	...
Mouth	16	1	6.3	3	...	...
Palate, uvula	1	....	...	.....	...	...
Pharynx	13	2	15.4	4	...	...
Salivary glands	.....	....	...	1	...	...
Teeth, gums, alveoli	15	....	...	8	...	...
Tongue	3	....	...	.....	...	...
Tonsils	225	4	1.8	183	2	1.1
Œsophagus	25	3	12.0	1	...	...
Pancreas	14	2	14.3	4	...	...
Rectum and anus	513	4	0.8	156	...	...
Stomach	230	7	3.0	99	4	4.0
Ductless glands and spleen	118	7	5.9	394	12	3.0
Carotid gland	.....	....	...	.....	...	...
Parathyreoid gland	.....	....	...	.....	...	...
Pineal gland	.....	....	...	.....	...	...
Pituitary body	15	1	6.7	19	1	5.3
Spleen	1	....	...	4	...	...
Suprarenal gland	16	3	18.8	3	...	...
Thymus gland	.....	....	...	.....	...	...
Thyreoid gland	86	3	3.5	368	11	3.0
Ear	82	6	7.3	56	2	3.6
Eye and adnexa	182	2	1.1	79	...	...
Infective diseases	2843	172	6.0	1262	75	5.9
Dysentery	135	6	4.4	13	1	7.7
Gonorrhœa	88	1	1.1	44	1	2.3
Influenza	86	....	...	38	...	...
Malaria	238	4	1.7	24	...	...
Rheumatic fever	70	3	4.3	15	...	...
Septicemia	20	15	75.0	18	8	44.4
Syphilis	266	6	2.3	73	2	2.7

TABLE 38. SUMMARY OF WHITE CASES—Continued.

	Males.			Females.		
Diseases and conditions.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Tuberculosis, meninges	27	19	70.4	16	13	81.3
Tuberculosis, lungs	312	24	7.7	154	9	5.8
Tuberculosis, miliary	5	4	80.0	3	3	100.0
Tuberculosis, other forms	483	18	3.7	334	13	3.9
Typhoid fever	695	52	7.5	307	18	5.9
Other infective diseases	418	20	4.8	223	7	3.1
Herniæ	903	18	2.0	229	14	6.1
Joints	386	3	0.8	265	2	0.8
Lymphatic system	101	2	2.0	43	2	4.7
Mind	292	8	2.7	274	1	0.4
Miscellaneous	770	54	7.0	834	24	2.9
Diabetes	128	7	5.5	69	5	7.2
Gout	41	1	2.4	4	...	...
Obesity	3	....	...	11	...	...
Rheumatism, ch. art	61	3	4.9	19	2	10.5
Rheumatism, n. s	11	....	...	7	1	14.3
Other miscellaneous	526	43	8.2	724	16	2.2
Muscles, fasciæ, tendons	102	2	2.0	48	1	2.1
Muscles and fasciæ	89	2	2.2	42	1	2.4
Tendons and sheaths	13	....	...	6	...	...
Nervous system	1518	69	4.5	1195	23	1.9
Brain, spinal cord, meninges	360	63	17.5	140	19	13.6
Cranial and spinal nerves	143	2	1.4	142	1	0.7
Functional nervous disorders	1015	4	0.4	913	3	0.3
Parasites	38	7	18.4	8	...	...
Poisonings and intoxications	137	7	5.1	40	4	10.0
Reproductive organs	1099	45	4.1	3472	40	1.2
Functional disorders	1	....	...	629	1	0.2
Mammary gland	.....	....	...	78	1	1.3
Ligaments, ovaries, tubes	.....	....	...	1256	27	2.1
Uterus	.....	....	...	856	4	0.5
Vagina	.....	....	...	611	7	1.1
Vulva	.....	....	...	42	...	...
Cowper's glands	.....	....	...	.....	...	...
Penis	19	....	...	.....	...	...
Prostate gland	767	43	5.6	.....	...	...
Scrotum	8	1	12.5	.....	...	...
Seminal vesicles	2	....	...	.....	...	...
Spermatic cord	105	....	...	.....	...	...
Testicle and epididymis	77	....	...	.....	...	...
Tunica vaginalis	120	1	0.8	.....	...	...
Respiratory system	840	90	10.7	291	25	8.6
Bronchi and trachea	175	5	2.9	79	4	5.1
Larynx and epiglottis	10	....	...	6	...	...
Lung	341	71	20.8	102	19	18.6
Nose and nasal passages	43	1	2.3	12	...	...
Accessory sinuses	13	1	7.7	5	...	...
Pleura	258	12	4.7	87	2	2.3
Skin, hair, nails	75	1	1.3	41	3	7.3
Skin and hair	72	1	1.4	37	3	8.1
Nails	3	....	...	4	...	...
Tumors	1496	205	13.7	1731	144	8.3
Benign	437	46	10.5	750	39	5.2
Malignant	1059	159	15.0	981	105	10.7

TABLE 38. SUMMARY OF WHITE CASES—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Urinary organs	881	100	11.4	757	42	5.5
Bladder	104	9	8.7	178	2	1.1
Kidney	575	83	14.4	521	40	7.7
Ureter	2	....	...	22	...	...
Urethra	200	8	4.0	36	...	...
Obstetrical conditions	.....	....	...	2973	59	2.0
Newborn child	2	....	...	.....	...	...
Injuries	1436	80	5.6	350	41	11.7
Grand total	17730	1235	7.0	16657	637	3.8

TABLE 39. WHITE MEDICAL CASES.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	13	....	...	6	1	16.7
Blood	177	42	23.7	68	13	19.1
Bones and cartilages	26	....	...	9	...	...
Bursæ	2	....	...	2	...	...
Circulatory system	1044	157	15.0	273	43	15.8
Arteries and veins	491	63	12.8	54	6	11.1
Endocardium and valves	395	71	18.0	179	29	16.2
Myocardium	120	16	13.3	27	6	22.2
Neuroses	24	2	8.3	5	...	...
Pericardium	14	5	35.7	8	2	25.0
Digestive system	760	31	4.1	421	8	1.9
Appendix	44	1	2.3	42	...	...
Intestine	129	6	4.7	80	4	5.0
Liver	154	16	10.4	24	2	8.3
Gall bladder and ducts	61	2	3.3	77	1	1.3
Mesentery	.....	....	...	.....	...	...
Omentum	.....	....	...	1	...	...
Peritoneum	4	1	25.0	7	1	14.3
Lips	.....	....	...	.....	...	...
Mouth	4	....	...	1	...	...
Palate, uvula	.....	....	...	.....	...	...
Pharynx	9	1	11.1	3	...	...
Salivary glands	.....	....	...	.....	...	...
Teeth, gums, alveoli	2	....	...	1	...	...
Tongue	1	....	...	.....	...	...
Tonsils	137	3	2.2	100	...	...
Œsophagus	9	....	...	.....	...	...
Pancreas	7	....	...	2	...	...
Rectum and anus	20	....	...	4	...	...
Stomach	179	1	0.6	79	...	...
Ductless glands and spleen	45	2	4.4	131	1	0.8
Carotid gland	.....	....	...	.....	...	...
Parathyreoid gland	.....	....	...	.....	...	...
Pineal gland	.....	....	...	.....	...	...
Pituitary body	2	....	...	1	...	...
Spleen	1	....	...	1	...	...

Table 39. White Medical Cases—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Suprarenal gland	13	2	15.4	3	...	...
Thymus gland	.....	....	...	.....	...	...
Thyreoid gland	29	....	...	126	1	0.8
Ear	15	....	...	6	...	...
Eye and adnexa	8	1	12.5	11	...	...
Infective diseases	2035	110	5.4	795	49	6.2
Dysentery	134	5	3.7	13	1	7.7
Gonorrhœa	43	....	...	18	1	5.6
Influenza	85	....	...	37	...	...
Malaria	235	4	1.7	24	...	...
Rheumatic fever	70	3	4.3	15	...	...
Septicemia	13	8	61.5	10	3	30.0
Syphilis	198	4	2.0	49	2	4.1
Tuberculosis, meninges	20	14	70.0	13	10	76.9
Tuberculosis, lungs	300	23	7.7	148	8	5.4
Tuberculosis, miliary	4	3	75.0	2	2	100.0
Tuberculosis, other forms	39	7	17.9	23	4	17.4
Typhoid fever	656	29	4.4	292	14	4.8
Other infective diseases	238	10	4.2	151	4	2.6
Herniæ	6	....	...	.....	...	...
Joints	186	2	1.1	131	...	...
Lymphatic system	23	2	8.7	7	...	...
Mind	272	8	2.9	264	1	0.4
Miscellaneous	406	29	7.1	201	15	7.5
Diabetes	125	6	4.8	66	5	7.6
Gout	41	1	2.4	4	...	...
Obesity	2	....	...	10	...	...
Rheumatism, ch. art	60	3	5.0	19	2	10.5
Rheumatism, n. s.	8	....	...	6	1	16.7
Other miscellaneous	170	19	11.2	96	7	7.3
Muscles, fasciæ, tendons	26	1	3.8	12	1	8.3
Muscles and fasciæ	26	1	3.8	12	1	8.3
Tendons and sheaths	.....	....	...	.....	...	...
Nervous system	1123	30	2.7	910	12	1.3
Brain, spinal cord, meninges	208	27	13.0	71	9	12.7
Cranial and spinal nerves	51	1	2.0	32	...	...
Functional nervous disorders	864	2	0.2	807	3	0.4
Parasites	7	....	...	6	...	...
Poisonings and intoxications	128	7	5.5	36	4	11.1
Reproductive organs	47	2	4.3	41	...	...
Functional disorders	.....	....	...	7	...	...
Mammary gland	.....	....	...	1	...	...
Ligaments, ovaries, tubes	.....	....	...	21	...	...
Uterus	.....	....	...	4	...	...
Vagina	.....	....	...	8	...	...
Vulva	.....	....	...	.....	...	...
Cowper's glands	.....	....	...	.....	...	...
Penis	1	....	...	.....	...	...
Prostate gland	36	2	5.6	.....	...	...
Scrotum	.....	....	...	.....	...	...
Seminal vesicles	.....	....	...	.....	...	...

TABLE 39. WHITE MEDICAL CASES—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Spermatic cord	.....	....	...	.....	...	...
Testicle and epididymis	10	....	...	.....	...	...
Tunica vaginalis	.....	....	...	.....	...	...
Respiratory system	657	77	11.7	222	23	10.4
Bronchi and trachea	166	4	2.4	73	4	5.5
Larynx and epiglottis	2	....	...	4	...	...
Lung	333	69	20.7	98	19	19.4
Nose and nasal passages	15	1	6.7	2	...	...
Accessory sinuses	.....	....	...	.....	...	...
Pleura	141	3	2.1	45	...	...
Skin, hair, nails	32	1	3.1	25	2	8.0
Skin and hair	32	1	3.1	25	2	8.0
Nails	.....	....	...	.....	...	...
Tumors	321	43	13.4	137	19	13.9
Benign	65	5	7.7	44	5	11.4
Malignant	256	38	14.8	93	14	15.1
Urinary organs	392	78	19.9	182	30	16.5
Bladder	20	5	25.0	13	...	...
Kidney	341	72	21.1	164	30	18.3
Ureter	.....	....	...	.....	...	...
Urethra	31	1	3.2	5	...	...
Obstetrical conditions	.....	....	...	22	1	4.5
Newborn child	.....	....	...	.....	...	...
Injuries	19	1	5.3	7	...	...
Grand total	7770	624	8.0	3925	223	5.7

TABLE 40. WHITE SURGICAL CASES.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	98	5	5.1	49	2	4.1
Blood	8	....	...	3	...	...
Bones and cartilages	363	7	1.9	124	5	4.0
Bursæ	25	....	...	10	...	...
Circulatory system	127	12	9.4	40	1	2.5
Arteries and veins	124	11	8.9	39	1	2.6
Endocardium and valves	2	....	...	1	...	...
Myocardium	.....	....	...	.....	...	...
Neuroses	.....	....	...	.....	...	...
Pericardium	1	1	100.0	.....	...	...
Digestive system	1786	103	5.8	866	38	4.4
Appendix	796	28	3.5	410	6	1.5
Intestine	123	22	17.9	61	10	16.4
Liver	35	13	37.1	9	3	33.3
Gall bladder and ducts	116	13	11.2	194	12	6.2
Mesentery	.....	....	...	.....	...	...
Omentum	.....	....	...	.....	...	...
Peritoneum	26	9	34.6	7	1	14.3
Lips	3	....	...	.....	...	...
Mouth	12	1	8.3	2	...	...

TABLE 40. WHITE SURGICAL CASES—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Palate, uvula	1	....	...	.....	...	...
Pharynx	4	1	25.0	1	...	...
Salivary glands	.....	....	...	1	...	...
Teeth, gums, alveoli	13	....	...	7	...	...
Tongue	2	....	...	.....	...	...
Tonsils	88	1	1.1	82	2	2.4
Œsophagus	16	3	18.8	1	...	...
Pancreas	7	2	28.6	2	...	...
Rectum and anus	493	4	0.8	70	...	...
Stomach	51	6	11.8	19	4	21.1
Ductless glands and spleen	73	5	6.8	261	11	4.2
Carotid gland	.....	....	...	.....	...	...
Parathyreoid gland	.....	....	...	.....	...	...
Pineal gland	.....	....	...	.....	...	...
Pituitary body	13	1	7.7	18	1	5.6
Spleen	.....	....	...	1	...	...
Suprarenal gland	3	1	33.3	.....	...	...
Thymus gland	.....	....	...	.....	...	...
Thyreoid gland	57	3	5.3	242	10	4.1
Ear	67	6	9.0	50	2	4.0
Eye and adnexa	174	1	0.6	68	...	...
Infective diseases	808	62	7.7	362	19	5.2
Dysentery	1	1	100.0	.....	...	...
Gonorrhæa	45	1	2.2	23	...	...
Influenza	1	....	...	1	...	...
Malaria	3	....	...	.....	...	...
Rheumatic fever	.....	....	...	.....	...	...
Septicemia	7	7	100.0	6	4	66.7
Syphilis	68	2	2.9	15	...	...
Tuberculosis, meninges	7	5	71.4	3	3	100.0
Tuberculosis, lungs	12	1	8.3	3	...	...
Tuberculosis, miliary	1	1	100.0	.....	...	...
Tuberculosis, other forms	444	11	2.5	243	5	2.1
Typhoid fever	39	23	59.0	11	4	36.4
Other infective diseases	180	10	5.6	57	3	5.3
Herniæ	897	18	2.0	127	11	8.7
Joints	200	1	0.5	132	2	1.5
Lymphatic system	78	....	...	30	2	6.7
Mind	20	....	...	10	...	...
Miscellaneous	364	25	6.9	127	8	6.3
Diabetes	3	1	33.3	1	...	...
Gout	.....	....	...	.....	...	...
Obesity	1	....	...	.....	...	...
Rheumatism, ch. art	1	....	...	.....	...	...
Rheumatism, n. s	3	....	...	.....	...	...
Other miscellaneous	356	24	6.7	126	8	6.3
Muscles, fasciæ, tendons	76	1	1.3	36	...	...
Muscles and fasciæ	63	1	1.6	30	...	...
Tendons and sheaths	13	....	...	6	...	...
Nervous system	395	39	9.9	250	11	4.4
Brain, spinal cord, meninges	152	36	23.7	69	10	14.5
Cranial and spinal nerves	92	1	1.1	109	1	0.9
Functional nervous disorders	151	2	1.3	72	...	...

TABLE 40. WHITE SURGICAL CASES—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Parasites	31	7	22.6	2	...	...
Poisonings and intoxications	9	....	...	1	...	...
Reproductive organs	1052	43	4.1	110	2	1.8
Functional disorders	1	....	...	3	...	...
Mammary gland	.....	....	...	77	1	1.3
Ligaments, ovaries, tubes	.....	....	...	24	1	4.2
Uterus	.....	....	...	3	...	...
Vagina	.....	....	...	3	...	...
Vulva	.....	....	...	.....	...	...
Cowper's glands	.....	....	...	.....	...	...
Penis	18	....	...	.....	...	...
Prostate gland	731	41	5.6	.....	...	...
Scrotum	8	1	12.5	.....	...	...
Seminal vesicles	2	....	...	.....	...	...
Spermatic cord	105	....	...	.....	...	...
Testicle and epididymis	67	....	...	.....	...	...
Tunica vaginalis	120	1	0.8	.....	...	...
Respiratory system	183	13	7.1	68	2	2.9
Bronchi and trachea	9	1	11.1	6	...	...
Larynx and epiglottis	8	....	...	2	...	...
Lung	8	2	25.0	3	...	...
Nose and nasal passages	28	....	...	10	...	...
Accessory sinuses	13	1	7.7	5	...	...
Pleura	117	9	7.7	42	2	4.8
Skin, hair, nails	43	....	...	13	1	7.7
Skin and hair	40	....	...	9	1	11.1
Nails	3	....	...	4	...	...
Tumors	1175	162	13.8	703	65	9.2
Benign	372	41	11.0	218	19	8.7
Malignant	803	121	15.1	485	46	9.5
Urinary organs	489	22	4.5	34	...	...
Bladder	84	4	4.8	2	...	...
Kidney	234	11	4.7	32	...	...
Ureter	2	....	...	.....	...	...
Urethra	169	7	4.1	.....	...	...
Obstetrical conditions	.....	....	...	4	...	...
Newborn child	2	....	...	.....	...	...
Injuries	1417	79	5.6	341	41	12.0
Grand total	9960	611	6.1	3821	223	5.8

TABLE 41. WHITE GYNECOLOGICAL CASES.

Diseases and conditions.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	7	...	...
Blood	4	...	...
Bones and cartilages	7	...	...
Bursæ	....	...	...
Circulatory system	2	...	...
Arteries and veins	2	...	...
Endocardium and valves	....	...	...
Myocardium	....	...	...
Neuroses	....	...	...
Pericardium	....	...	...

TABLE 41. WHITE GYNECOLOGICAL CASES—Continued.

Diseases and conditions.	Admitted.	Died.	Per cent.
Digestive system	424	12	2.8
Appendix	226	2	0.9
Intestine	27	3	11.1
Liver	3	...	...
Gall bladder and ducts	40	2	5.0
Mesentery	....	...	...
Omentum	2	...	...
Peritoneum	42	5	11.9
Lips	....	...	...
Mouth	....	...	...
Palate, uvula	....	...	...
Salivary glands	....	...	...
Teeth, gums, alveoli	....	...	...
Tongue	....	...	...
Tonsils	1	...	...
Œsophagus	....	...	...
Pancreas	....	...	...
Rectum and anus	82	...	...
Stomach	1	...	...
Ductless glands and spleen	2	...	...
Carotid gland	....	...	...
Parathyroid gland	....	...	...
Pineal gland	....	...	...
Pituitary body	....	...	...
Spleen	2	...	...
Suprarenal gland	....	...	...
Thymus gland	....	...	...
Thyreoid gland	....	...	...
Ear	....	...	...
Eye and adnexa	....	...	...
Infective diseases	105	7	6.7
Dysentery	....	...	...
Gonorrhœa	3	...	...
Influenza	....	...	...
Malaria	....	...	...
Rheumatic fever	....	...	...
Septicemia	2	1	50.0
Syphilis	9	...	...
Tuberculosis, meninges	....	...	...
Tuberculosis, lungs	3	1	33.3
Tuberculosis, miliary	1	1	100.0
Tuberculosis, other forms	68	4	5.9
Typhoid fever	4	...	...
Other infective diseases	15	...	...
Herniæ	102	3	2.9
Joints	2	...	...
Lymphatic system	6	...	...
Mind	....	...	...
Miscellaneous	506	1	0.2
Diabetes	2	...	...
Gout	....	...	...
Obesity	1	...	...
Rheumatism, ch. art	....	...	...
Rheumatism, n. s	1	...	...
Other miscellaneous	502	1	0.2

TABLE 41. WHITE GYNECOLOGICAL CASES—Continued.

Diseases and conditions.	Admitted.	Died.	Per cent.
Muscles, fasciæ, tendons	....	...	...
Muscles and fasciæ	....	...	...
Tendons and sheaths	....	...	...
Nervous system	35	...	...
Brain, spinal cord, meninges	....	...	...
Cranial and spinal nerves	1	...	...
Functional nervous disorders	34	...	...
Parasites	....	...	...
Poisonings and intoxications	3	...	...
Reproductive organs	3321	38	1.1
Functional disorders	619	1	0.2
Mammary gland	....	...	...
Ligaments, ovaries, tubes	1211	26	2.1
Uterus	849	4	0.5
Vagina	600	7	1.2
Vulva	42	...	...
Cowper's glands	....	...	...
Penis	....	...	...
Prostate gland	....	...	...
Scrotum	....	...	...
Seminal vesicles	....	...	...
Spermatic cord	....	...	...
Testicle and epididymis	....	...	...
Tunica vaginalis	....	...	...
Respiratory system	1	...	...
Bronchi and trachea	....	...	...
Larynx and epiglottis	....	...	...
Lung	1	...	...
Nose and nasal passages	....	...	...
Accessory sinuses	....	...	...
Pleura	....	...	...
Skin, hair, nails	3	...	...
Skin and hair	3	...	...
Nails	....	...	...
Tumors	891	60	6.7
Benign	488	15	3.1
Malignant	403	45	11.2
Urinary organs	541	12	2.2
Bladder	163	2	1.2
Kidney	325	10	3.1
Ureter	22	...	...
Urethra	31	...	...
Obstetrical conditions	462	8	1.7
Newborn child	....	...	...
Injuries	2	...	...
Grand total	6426	141	2.2

TABLE 42. WHITE MEDICAL CASES.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abdominal pain	9	...	....	12	...	....
Abortion	...	...	....	1	...	....
Abscess, alveolar	1	...	....	...	...	....
Abscess, breast	...	...	....	1	...	....
Abscess, chest wall	1	...	....	1	...	....
Abscess, gluteal	1	...	....	...	...	....
Abscess, intra-abdominal	1	...	....	...	...	....
Abscess, kidney	1	...	....	...	...	....
Abscess, leg	1	...	....	1	...	....
Abscess, liver	15	...	....	1	1	100.0
Abscess, lung	4	1	25.0	2	1	50.0
Abscess, mastoid	1	...	....	...	...	....
Abscess, mediastinal	1	...	....	...	...	....
Abscess, multiple	...	...	....	1	...	....
Abscess, pancreas	...	...	....	1	...	....
Abscess, pelvic	...	...	....	1	...	....
Abscess, perinephritic	6	...	....	1	...	....
Abscess, perirectal	1	...	....	...	...	....
Abscess, perirenal	5	...	....	...	...	....
Abscess, peritoneum	...	...	....	1	...	....
Abscess, peritonsillar	2	...	....	...	...	....
Abscess, periurethral	2	...	....	...	...	....
Abscess, prostatic	1	...	....	...	...	....
Abscess, retroperitoneal	1	...	....	...	...	....
Abscess, subdiaphragmatic	1	...	....	...	...	....
Abscess, subphrenic	1	...	....	...	...	....
Abscess, thigh	1	...	....	...	...	....
Abscess, tonsillar	2	1	50.0	1	...	....
Achlorhydria	2	...	....	...	...	....
Achylia gastrica	1	...	....	1	...	....
Acrocyanosis	8	...	....	2	...	....
Acromegaly	2	...	....	1	...	....
Acroparesthesia chronica	...	...	....	1	...	....
Addison's disease	8	2	25.0	3	...	....
Adenitis	9	...	....	7	...	....
Adenocarcinoma, stomach	1	...	....	...	...	....
Adenoids	9	...	....	1	...	....
Adhesions	2	...	....	6	...	....
Adhesions, omental	...	...	....	1	...	....
Adiposis dolorosa	2	...	....	10	...	....
Aerophagia, hysterical	...	...	....	1	...	....
Albuminuria	6	...	....	...	...	....
Alcoholism	62	7	11.3	8	...	....
Amblyopia, tobacco	1	...	....	...	...	....
Amenorrhœa	...	...	....	1	...	....
Anacidity	6	...	....	3	...	....
Anæmia, aplastic	2	...	....	...	...	....
Anæmia, pernicious	99	23	23.2	25	7	28.0
Anæmia, secondary	6	2	33.3	9	...	....
Anæmia, splenic	10	1	10.0	4	...	....
Aneurism, abdominal	5	2	40.0	...	...	....
Aneurism, aortic	42	4	9.5	...	...	....
Aneurism, arteriovenous	2	...	....	...	...	....
Aneurism, cirsoid	1	...	....	...	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Aneurism, thoracic	45	4	8.9	6	2	33.3
Angina, pseudo-	2	...	....	...	...	....
Angiomata	1	...	....	...	...	....
Anorexia nervosa	4	...	....	10	...	....
Aphasia	1	...	....	...	...	....
Aphasia, motor	2	...	....	...	...	....
Aphonia, hysterical	...	...	....	2	...	....
Appendicitis	44	1	2.3	42	...	....
Argyria	1	...	....	...	...	....
Arrested sexual development	1	...	....	...	...	....
Arteriosclerosis	363	51	14.0	42	4	9.5
Arthritis	12	...	....	9	...	....
Arthritis deformans	89	1	1.1	81	...	....
Arthritis, gonorrhœal	34	...	....	12	...	....
Arthritis, hypertrophic	5	...	....	4	...	....
Arthritis, infectious	35	1	2.9	22	...	....
Arthritis, knee	1	...	....	...	...	....
Arthritis, rheumatoid	1	...	....	...	...	....
Arthritis, villous	2	...	....	...	...	....
Ascites	1	1	100.0	2	...	....
Asphyxia	...	...	....	1	...	....
Asthenia	1	...	....	...	...	....
Asthma	41	...	....	18	...	....
Astigmatism, myopic	1	...	....	...	...	....
Asynergy, cerebellar	5	...	....	...	...	....
Ataxia, cerebellar	1	...	....	...	...	....
Ataxia, Friedreich's	...	...	....	2	...	....
Ataxia, locomotor	18	1	5.6	3	...	....
Atrophy, muscular	18	1	5.6	6	1	16.7
Bacilluria	3	...	....	2	...	....
Bacteriuria	1	...	....	...	...	....
Banti's disease	1	...	....	...	...	....
Brachialgia	...	...	....	1	...	....
Bronchiectasis	16	2	12.5	4	1	25.0
Bronchitis	79	...	....	44	3	6.8
Bubo, inguinal	4	...	....	...	...	....
Burns	...	...	....	2	...	....
Bursitis	2	...	....	2	...	....
Calculus, biliary	49	2	4.1	73	1	1.4
Calculus, renal	23	...	....	10	...	....
Calculus, urethral	1	...	....	...	...	....
Carcinoma, bile passages	4	...	....	6	1	16.7
Carcinoma, breast	1	...	....	5	...	....
Carcinoma, cæcum	1	...	....	...	...	....
Carcinoma, cervix uteri	...	...	....	2	...	....
Carcinoma, colon	1	...	....	1	1	100.0
Carcinoma, face	1	...	....	...	...	....
Carcinoma, gall bladder	...	...	....	3	2	66.7
Carcinoma, glands neck	1	...	....	...	...	....
Carcinoma, ilium	...	...	....	1	...	....
Carcinoma, intestine	6	...	....	2	1	50.0
Carcinoma, kidney	2	...	....	...	...	....
Carcinoma, latent	1	...	....	...	...	....
Carcinoma, liver	12	2	16.7	3	...	....

Table 42. White Medical Cases—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Carcinoma, lung	2	2	100.0	1	...	....
Carcinoma, œsophagus	9	3	33.3	2	1	50.0
Carcinoma, ovary	...	...	....	1	...	....
Carcinoma, pancreas	5	...	....	6	...	....
Carcinoma, pelvis	2	...	....	1	1	100.0
Carcinoma, prostate	11	1	9.1	...	...	....
Carcinoma, rectum	8	...	....	2	...	....
Carcinoma, sigmoid flexure	1	...	....	1	...	....
Carcinoma, stomach	135	18	13.3	33	4	12.1
Carcinoma, submaxillary gland	1	...	....	...	...	....
Carcinoma, thyroid gland	...	...	....	1	...	....
Carcinoma, tongue	1	...	....	...	...	....
Carcinoma, tonsil	1	...	....	...	...	....
Carcinoma, uterus	...	...	....	1	...	....
Carcinoma, ventriculi	12	2	16.7	6	...	....
Carcinoma, vertebræ	1	...	....	1	1	100.0
Carcinomatosis, general	1	...	....	2	...	....
Carcinosis	2	...	....	...	...	....
Caries, spine	1	...	....	...	...	....
Catarrh, nasal	1	...	....	...	...	....
Cellulitis	4	...	....	1	1	100.0
Cephalalgia	3	...	....	5	...	....
Chancroid	1	...	....	...	...	....
Chlorosis	...	...	....	6	...	....
Cholangitis	2	...	....	...	...	....
Cholecystitis	10	...	....	4	...	....
Cholera infantum	...	...	....	1	1	100.0
Chorea	22	1	4.5	42	1	2.4
Cirrhosis, liver	91	16	17.6	16	1	6.3
Cirrhosis, stomach	1	...	....	...	...	....
Coccygodynia	...	...	....	1	...	....
Coccyxitis	...	...	....	1	...	....
Colic, intestinal	1	...	....	...	...	....
Colic, renal	4	...	....	...	...	....
Colitis	14	1	7.1	22	1	4.5
Colitis, polypoid	1	...	....	...	...	....
Colitis, ulcerative	2	...	....	...	...	....
Coloptosis	1	...	....	...	...	....
Coma	1	...	....	1	...	....
Conjunctivitis	1	...	....	6	...	....
Constipation	14	...	....	8	...	....
Contusion	2	...	....	...	...	....
Convalescence	6	...	....	19	1	5.3
Convulsions, infantile	...	...	....	4	...	....
Coxalgia	1	...	....	...	...	....
Coxa valga	...	...	....	1	...	....
Cretinism	1	...	....	2	...	....
Crushed hand	1	...	....	...	...	....
Cyanosis	2	...	....	...	...	....
Cyst, breast	...	...	....	1	...	....
Cyst, cerebellum	2	2	100.0	...	...	....
Cyst, liver	...	...	....	1	...	....
Cyst, ovarian	...	...	....	6	1	16.7
Cyst, renal	5	1	20.0	1	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Cystinuria	1	...	....	...	...	....
Cystitis	16	5	31.3	11	...	....
Dementia	6	...	....	...	...	....
Dementia, alcoholic	2	...	....	...	...	....
Dementia paralytica	3	...	....	...	...	....
Dementia præcox	11	...	....	9	...	....
Dementia, senile	1	...	....	1	...	....
Dermatitis	2	...	....	1	...	....
Deviation nasal septum	1	...	....	...	...	....
Diabetes insipidus	3	...	....	...	...	....
Diabetes mellitus	122	6	4.9	66	5	7.6
Diarrhœa	38	1	2.6	13	...	....
Dilatation, aorta	7	...	....	...	...	....
Dilatation, colon	1	...	....	...	...	....
Dilatation, duodenum	...	...	....	1	...	....
Dilatation, stomach	9	...	....	4	...	....
Diphtheria	58	3	5.2	64	3	4.7
Diplegia	1	...	....	1	...	....
Diplegia, spastic	...	...	....	1	...	....
Displacement, kidney	1	...	....	...	...	....
Disturbance, glands of internal secretion	...	...	....	2	...	....
Drug habit	...	...	....	1	...	....
Dysentery	10	1	10.0	2	...	....
Dysentery, amœbic	123	4	3.3	11	1	9.1
Dysentery, chronic	1	...	....	...	...	....
Dysmenorrhœa	...	...	....	2	...	....
Dyspepsia	11	...	....	...	...	....
Dyspepsia, nervous	36	...	....	22	...	....
Dystrophy, muscular	1	...	....	...	...	....
Eczema	4	...	....	5	...	....
Elephantiasis	1	...	....	...	...	....
Emphysema	30	2	6.7	7	...	....
Empyema	29	1	3.4	8	1	12.5
Encephalitis	2	...	....	2	...	....
Encephalomalacia	1	1	100.0	...	...	....
Encephalo-myelitis	...	...	....	1	...	....
Endothelioma, lung	1	1	100.0	...	...	....
Enlarged liver	1	...	....	...	...	....
Enlarged prostate	4	...	....	...	...	....
Enlarged spleen	1	...	....	1	...	....
Enlarged thyroid	...	...	....	1	...	....
Enlarged tonsils	1	...	....	...	...	....
Enteritis	12	1	8.3	2	...	....
Enterocolitis	2	2	100.0	...	...	....
Enteroptosis	1	...	....	12	...	....
Epididymitis	6	...	....	...	...	....
Epilepsy	54	...	....	17	...	....
Epilepsy, Jacksonian	2	...	....	...	...	....
Epistaxis	3	1	33.3	...	...	....
Epithelioma	1	...	....	...	...	....
Epithelioma, œsophagus	1	1	100.0	...	...	....
Epithelioma, tonsil	1	1	100.0	...	...	....
Error of refraction	...	...	...	1	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Erysipelas	10	1	10.0	9	...	....
Erythema	4	...	....	7	...	....
Erythromelalgia	2	...	....	...	...	....
Ethmoiditis	1	...	....	1	...	....
Febricula	85	...	....	29	...	....
Fecal impaction	...	...	....	1	...	....
Fever, continuous	43	...	....	17	...	....
Fever, ephemeral	1	...	....	...	...	....
Fever, glandular	2	...	....	...	...	....
Fever, malarial	235	4	1.7	24	...	....
Fever, paratyphoid	2	...	....	3	...	....
Fever, remittent	1	...	....	...	...	....
Fever, rheumatic	70	3	4.3	15	...	....
Fever, scarlet	6	...	....	7	...	....
Fever, typhoid	606	29	4.8	271	14	5.2
Fever, typhus	3	...	....	...	...	....
Fever, unknown cause	1	...	....	1	...	....
Fibroma	...	...	....	1	...	....
Fibroma, ovary	...	...	....	1	...	....
Fibro-sarcoma, spinal cord	1	...	....	...	...	....
Fistula, œsophageal	2	...	....	...	...	....
Foreign body in eye	1	...	....	...	...	....
Fracture, femur	2	...	....	...	...	....
Fracture, lumbar vertebræ	2	...	....	...	...	....
Furunculosis	1	...	....	2	...	....
Gangrene	1	...	....	...	...	....
Gangrene, toes and feet	1	...	....	...	...	....
Gastralgia	...	...	....	1	...	....
Gastrectasis	1	...	....	...	...	....
Gastritis	30	...	....	7	...	....
Gastro-enteritis	19	...	....	8	1	12.5
Geographical tongue	1	...	....	...	...	....
Giant colon	1	...	....	1	...	....
Gigantism	1	...	....	...	...	....
Glaucoma	...	...	....	1	...	....
Glycosuria	1	...	....	1	...	....
Goitre	1	...	....	6	...	....
Goitre, colloid	1	...	....	...	...	....
Goitre, exophthalmic	19	...	....	81	1	1.2
Gonorrhœa	4	...	....	...	...	....
Gout	41	1	2.4	4	...	....
Gumma	1	...	....	...	...	....
Gumma, testicle	1	...	....	...	...	....
Heart diseases:						
Adherent pericardium	1	1	100.0	1	1	100.0
Angina pectoris	10	1	10.0	1	...	....
Arrhythmia	2	...	....	2	...	....
Bradycardia	1	...	....	...	...	....
Congenital	4	...	....	2	1	50.0
Endocarditis	38	21	55.3	12	4	33.3
Hypertrophy	2	...	....	...	...	....
Myocarditis	98	15	15.3	22	6	27.3
Neurosis	...	...	....	1	...	....
Pericarditis	11	3	27.3	6	1	16.7

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Pericarditis, tuberculous	2	1	50.0	...	...	....
Stokes-Adams disease	4	...	....	1	...	....
Tachycardia	10	1	10.0	2	...	....
Aortic dilatation	1	...	....	...	...	....
Aortic insufficiency	53	10	18.9	6	1	16.7
Aortic insufficiency and stenosis	1	1	100.0	...	...	....
Aortic and mitral insufficiency	75	12	16.0	16	2	12.5
Aortic insufficiency, mitral insufficiency and stenosis	18	2	11.1	8	1	12.5
Aortic, mitral, myocardial insufficiency	8	...	....	3	...	....
Aortic, myocardial insufficiency	2	1	50.0	...	...	....
Aortic, mitral, tricuspid insufficiency	1	...	....	...	...	....
Aortic and mitral insufficiency and stenosis	6	1	16.7	4	...	....
Aortic insufficiency, mitral insufficiency and stenosis	12	2	16.7	4	1	25.0
Aortic insufficiency and mitral stenosis	5	1	20.0	1	...	....
Aortic insufficiency and stenosis, mitral insufficiency and stenosis	4	1	25.0	...	...	....
Aortic stenosis	1	...	....	1	1	100.0
Aortic stenosis and insufficiency	9	1	11.1	1	1	100.0
Aortic and mitral stenosis	1	...	....	1	1	100.0
Aortic stenosis, mitral insufficiency	3	...	....	1	...	....
Mitral insufficiency	69	5	7.2	32	4	12.5
Mitral insufficiency and stenosis	54	11	20.4	53	7	13.2
Mitral and myocardial insufficiency	9	...	....	3	1	33.3
Mitral, myocardial insufficiency mitral stenosis	3	...	....	1	...	....
Mitral stenosis	20	2	10.0	28	2	7.1
Mitral and tricuspid insufficiency and stenosis	...	...	....	1	1	100.0
Mitral and tricuspid insufficiency	...	...	....	1	...	....
Mitral stenosis and tricuspid insufficiency	1	...	....	...	...	....
Mitral and tricuspid insufficiency and stenosis	...	...	....	2	2	100.0
Myocardial insufficiency	13	1	7.7	2	...	....
Myocardial insufficiency, mitral stenosis	3	...	....	1	...	....
Tricuspid insufficiency and stenosis	1	...	....	...	...	....
Pulmonary stenosis	...	...	....	1	...	....
Heat prostration	6	1	16.7	1	...	....
Hebephrenia	1	...	....	...	...	....
Hemachromatosis	8	3	37.0	...	...	....
Hematemesis	3	...	....	...	...	....
Hematoporphyrinuria	...	...	....	2	...	....
Hematuria	10	...	....	5	...	....
Hemianopsia	1	...	....	...	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Hemichorea	...	...	....	1	...	....
Hemicrania	...	...	....	1	...	....
Hemiplegia	29	3	10.3	12	1	8.3
Hemophilia	8	...	....	...	...	....
Hemoptysis	3	...	....	1	...	....
Hemorrhage, cerebral	7	4	57.1	...	...	....
Hemorrhoids	12	...	....	3	...	....
Hernia	3	...	....	...	...	....
Hernia, inguinal	2	...	....	...	...	....
Hernia, strangulated	1	...	....	...	...	....
Herpes zoster	3	...	....	3	...	....
Hodgkin's disease	11	2	18.2	...	...	....
Hydrocele	1	...	....	...	...	....
Hydrocephalus	6	1	16.7	...	...	....
Hydrocystoma	...	...	....	1	...	....
Hydronephrosis	4	...	....	1	...	....
Hydrosalpinx	...	...	....	1	...	....
Hyperacidity	21	...	....	6	...	....
Hyperchlorhydria	2	...	....	1	...	....
Hypernephrosis	...	...	....	3	...	....
Hyperthyroidism	5	...	....	27	...	....
Hypertrophy, liver	2	...	....	...	...	....
Hypertrophy, prostate	3	1	33.3	...	...	....
Hypertrophy, uterus	...	...	....	1	...	....
Hypochondriasis	3	...	....	...	...	....
Hysteria	16	...	....	78	1	1.3
Ichthyosis hystrix	...	...	....	1	...	....
Icterus	...	...	....	1	...	....
Idiocy	2	...	....	1	...	....
Imbecility	...	...	....	1	...	....
Inanition	2	...	....	...	...	....
Infection, hand	2	...	....	...	...	....
Inflammation, heels	1	...	....	...	...	....
Influenza	83	...	....	37	...	....
Injury, foot	1	...	....	...	...	....
Insanity, manic depressive	10	...	....	19	...	....
Insomnia	3	...	....	1	...	....
Intestinal obstruction	7	1	14.1	1	1	100.0
Intussusception	1	...	....	1	...	....
Irido-cyclitis	1	...	....	...	...	....
Jaundice	1	...	....	1	...	....
Jaundice, catarrhal	41	...	....	5	...	....
Jaundice, obstructive	4	...	....	...	...	....
Kyphosis	...	...	....	1	...	....
Laryngitis	1	...	....	4	...	....
Laryngitis, syphilitic	1	...	....	...	...	....
Leptomeningitis	...	...	....	1	1	100.0
Leucorrhœa	...	...	....	1	...	....
Leukæmia	13	5	38.5	7	1	14.3
Leukæmia, lymphatic	7	4	57.1	2	1	50.0
Leukæmia, splenomyelogenous	13	4	30.8	4	1	25.0
Lipomatosis	1	...	....	2	...	....
Lues	22	1	4.5	4	...	....
Lues, cerebral	14	1	7.1	4	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Lues, congenital	1	...	....	...	...	....
Lues, liver	1	...	....	...	...	....
Lues, secondary	6	...	....	2	...	....
Lues, tertiary	16	...	....	4	...	....
Lumbago	2	...	....	...	...	....
Lumbar pain	1	...	....	...	...	....
Lupus	1	...	....	...	...	....
Lymphadenitis	1	...	....	...	...	....
Lymphomatosis	...	...	....	1	1	100.0
Lympho-sarcoma	5	1	20.0	1	...	....
Malaise	1	...	....	...	...	....
Malformation, urethra	1	1	100.0	...	...	....
Malingering	1	...	....	...	...	....
Malnutrition	1	...	....	3	...	....
Mania, acute	...	...	....	2	...	....
Marasmus	...	...	....	1	...	....
Mastitis	...	...	....	1	...	....
Mastoiditis, acute	2	...	....	1	...	....
Measles	9	...	....	19	...	....
Melancholia	9	...	....	7	1	14.3
Melena	1	...	....	...	...	....
Meningitis	5	...	....	1	...	....
Meningitis, cerebrospinal	30	13	43.3	13	7	53.8
Meningitis, streptococcus	...	...	....	1	...	....
Merycismus	1	...	....	...	...	....
Microcephaly	...	...	....	1	...	....
Migraine	3	...	....	4	...	....
Monoplegia	2	...	....	...	...	....
Morphinism	21	...	....	6	...	....
Myalgia	1	...	....	...	...	....
Myasthenia gravis	1	...	....	1	...	....
Myelitis	8	1	12.5	4	...	....
Myoma	...	...	....	1	...	....
Myoma, uterus	...	...	....	1	...	....
Myxœdema	2	...	....	9	...	....
Necrosis, rib	1	...	....	...	...	....
Neoplasm	2	...	....	5	...	....
Neoplasm, intrathoracic	...	...	....	1	...	....
Neoplasm, rectum	1	...	....	...	...	....
Nephritis	269	69	25.6	130	26	20.0
Nephritis, parenchymatous	...	...	....	1	...	....
Nephroptosis	1	...	....	1	...	....
Neuralgia	9	...	....	7	...	....
Neuralgia, brachial	1	...	....	1	...	....
Neuralgia, supraorbital	...	...	....	1	...	....
Neuralgia, trifacial	...	...	....	1	...	....
Neurasthenia	693	...	....	636	...	....
Neuritis	12	...	....	11	...	....
Neuritis, alcoholic	5	...	....	...	...	....
Neuritis, arsenical	1	...	....	...	...	....
Neuritis, ascending	1	1	100.0	...	...	....
Neuritis, multiple	3	...	....	...	...	....
Neuritis, optic	2	...	....	...	...	....
Neuritis, peripheral	4	...	....	1	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

	Males.			Females.		
Causes.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Neurofibromata, multiple	...	...	....	2	...	....
Neurosis	36	...	....	6	...	....
Neurosis, traumatic	1	...	....	...	...	....
Neurosis, vasomotor	...	...	....	1	...	....
Nevus telangiectatic	1	...	....	...	...	....
Œdema	2	1	100.0	1	...	....
Œdema, angioneurotic	4	...	....	4	...	....
Œsophageal diverticulum	1	...	....	...	...	....
Œsophageal obstruction	2	...	....	...	...	....
Ophthalmoplegia	1	1	100.0	...	...	....
Orthopnea, paroxysmal	1	...	....	...	...	....
Osteitis deformans	1	...	....	...	...	....
Osteoarthritis	11	...	....	5	...	....
Osteoarthropathy, hypertrophic pulmonary	1	...	....	...	...	....
Osteoma	1	...	....	1	...	....
Osteomyelitis	4	...	....	1	...	....
Otitis media	12	...	....	5	...	....
Pachymeningitis	1	...	....	...	...	....
Painful hip	1	...	....	1	...	....
Palsy	2	...	....	...	...	....
Pancreatitis	6	...	....	1	...	....
Pancreatitis, gangrenous	1	...	....	...	...	....
Papilloma	2	...	....	...	...	....
Papilloma, rectum	1	...	....	...	...	....
Paralysis	21	1	4.8	11	...	....
Paralysis, facial	3	...	....	...	...	....
Paralysis, post-diphtheritic	3	1	33.3	...	...	....
Paralysis, spastic	...	...	....	1	...	....
Paramyoclonus multiplex	2	...	....	...	...	....
Paranoia	...	...	....	2	...	....
Paraplegia	2	...	....	1	...	....
Paraplegia, ataxic	2	...	....	...	...	....
Paraplegia, hysterical	...	...	....	1	...	....
Paraplegia, spastic	10	...	....	2	...	....
Parasites, intestinal	3	...	....	6	...	....
Paregoric habit	...	...	....	1	...	....
Paresis	23	...	....	1	...	....
Paresis, general	11	1	9.1	1	...	....
Parotitis	20	1	5.0	9	...	....
Pellagra	10	1	10.0	4	...	....
Pelvic inflammatory disease	...	...	....	3	...	....
Pemphigus foliaceus	3	...	....	...	...	....
Pemphigus vegetans	...	...	....	4	2	50.0
Periostitis	3	...	....	1	...	....
Peritonitis, general	3	1	33.3	6	1	16.7
Pertussis	5	1	20.0	...	...	....
Pharyngitis	9	1	11.1	3	...	....
Phimosis	1	...	....	...	...	....
Phlebitis	7	1	14.3	...	...	....
Phlebitis, post-typhoid	1	...	....	...	...	....
Phlegmon, neck	1	...	....	...	...	....
Pleurisy	33	1	3.0	8	...	....
Pleurisy, diaphragmatic	...	...	....	1	...	....

Table 42. White Medical Cases—Continued.

	Males.			Females.		
Causes.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Pleurisy, fibrinous	33	...	....	13	...	....
Pleurisy with effusion	66	2	3.0	23	...	....
Pleurodynia	1	...	....	...	...	....
Pneumonia, bronchial	34	13	38.2	21	3	14.3
Pneumonia, influenzal	2	...	....	...	...	....
Pneumonia, lobar	263	54	20.5	66	14	21.2
Pneumonia, tuberculous	3	...	....	1	...	....
Pneumothorax	2	...	....	...	...	....
Poisoning, acetanilide	1	...	....	...	...	....
Poisoning, arsenic	2	...	....	...	...	....
Poisoning, atropine	1	...	....	...	...	....
Poisoning, bichloride of mercury	2	...	....	1	...	....
Poisoning, carbolic acid	6	2	33.3	4	1	25.0
Poisoning, carbon monoxide	3	...	....	1	...	....
Poisoning, chloroform	1	1	100.0	...	...	....
Poisoning, drug	1	...	....	...	...	....
Poisoning, gas	5	1	20.0	4	...	....
Poisoning, lead	37	...	....	1	...	....
Poisoning, lye	1	...	....	...	...	....
Poisoning, mercurial	2	...	....	1	1	100.0
Poisoning, morphine	1	1	100.0	2	...	....
Poisoning, oil sassafras	1	...	....	...	...	....
Poisoning, opium	6	1	16.7	4	...	....
Poisoning, paraldehyde	...	...	....	1	1	100.0
Poisoning, potassium cyanide	1	...	....	...	...	....
Poisoning, ptomaine	2	...	....	1	...	....
Poisoning, salicylic acid	...	...	....	1	...	....
Poisoning, strychnia	1	...	....	...	...	....
Poisoning, vegetable	1	...	....	...	...	....
Poisoning, wood alcohol	...	...	....	1	1	100.0
Poliomyelitis	6	...	....	6	...	....
Polyarthritis	3	...	....	...	...	....
Polyarthritis, gonorrhœal	5	...	....	4	...	....
Polyarthritis, infectious	5	...	....	4	...	....
Polycythæmia	5	1	20.0	3	1	33.3
Polypi, larynx	1	...	....	...	...	....
Polypi, nasal	1	...	....	...	...	....
Polyserositis	4	...	....	1	...	....
Pregnancy	...	...	....	18	...	....
Proctitis	3	...	....	...	...	....
Prolapsus, colon	...	...	....	1	...	....
Prolapsus recti	2	...	....	...	...	....
Prostatitis	28	1	3.6	...	...	....
Pruritus	...	...	....	1	...	....
Pseudo-cyesis	...	...	....	1	...	....
Pseudo-tabes	2	...	....	...	...	....
Psoriasis	4	...	....	...	...	....
Psychasthenia	101	...	....	159	...	....
Psychoneurosis	24	...	....	48	...	....
Psychosis	6	...	....	6	...	....
Psychosis, post-typhoid	1	...	....	...	...	....
Purpura	3	...	....	1	...	....
Purpura hemorrhagica	...	...	....	2	2	100.0
Purpura, Henoch's	4	1	25.0	3	...	....

Table 42. White Medical Cases—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Purpura rheumatica	2	...	....	...	...	....
Purpura simplex	1	...	....	2	...	....
Pyæmia	...	...	....	1	...	....
Pyelitis	7	...	....	8	1	12.5
Pyelonephritis	...	...	....	1	...	....
Pyonephrosis	1	...	....	...	...	....
Pyorrhœa alveolaris	1	...	....	1	...	....
Pyuria	1	...	....	...	...	....
Quinsy	3	...	....	6	...	....
Rachitis	1	...	....	...	...	....
Raynaud's disease	5	...	....	2	1	50.0
Recklinghausen's disease	1	...	....	...	...	....
Relaxation, joint	2	...	....	...	...	....
Relaxed vagina	...	...	....	4	...	....
Retinitis	...	...	....	1	...	....
Retroflexion, uterus	...	...	....	2	...	....
Retroversion, uterus	...	...	....	1	...	....
Rheumatism	8	...	....	6	1	16.7
Rheumatism, articular	60	3	5.0	19	2	10.5
Rhinitis	...	...	....	1	...	....
Salpingo-oophoritis	...	...	....	17	...	....
Sarcoma, cerebrum	1	1	100.0	...	...	....
Sarcoma, cervical gland	1	...	....	...	...	....
Sarcoma, ileum	1	...	....	...	...	....
Sarcoma, intra-nasal	1	...	....	...	...	....
Sarcoma, intra-thoracic	1	1	100.0	...	...	....
Sarcoma, kidney	3	...	....	...	...	....
Sarcoma, liver	2	2	100.0	...	...	....
Sarcoma, lymph-glands	...	...	....	1	1	100.0
Sarcoma, osteo-	2	...	....	...	...	....
Sarcoma, prostate	1	...	....	...	...	....
Sarcoma, retroperitoneal	5	2	40.0	...	...	....
Sarcoma, spinal cord	1	...	....	...	...	....
Sarcoma, sternum	1	...	....	...	...	....
Sarcomatosis	...	...	....	1	1	100.0
Schönlein's disease	6	...	....	2	...	....
Sciatica	8	...	....	3	...	....
Scleroderma	2	...	....	1	...	....
Sclerosis	6	...	....	10	...	....
Sclerosis, lateral	1	...	....	...	...	....
Sclerosis, multiple	5	...	....	3	...	....
Scoliosis	...	...	....	1	...	....
Scurvy	4	...	....	1	...	....
Senility	8	...	....	...	...	....
Septicemia	11	8	72.7	9	3	33.3
Septicemia, gonococcus	...	...	....	2	1	50.0
Septicemia, puerperal	...	...	....	1	1	100.0
Serum disease	...	...	....	1	...	....
Singultus	1	...	....	...	...	....
Sinusitis	13	...	....	1	...	....
Smallpox	2	...	....	2	...	....
Spasm, intestinal	1	...	....	...	...	....
Splanchnoptosis	...	...	....	1	...	....
Splenomegaly	9	2	22.2	3	...	....

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Spondylitis	12	...	....	1	...	....
Spondylitis deformans	5	...	....	...	...	....
Spondylitis, infectious	3	...	....	...	...	....
Spondylolisthesis	...	...	....	1	...	....
Sprain	2	...	....	1	...	....
Stenosis, pyloric	10	1	10.0	2	...	....
Stenosis, rectal	1	...	....	...	...	....
Stomach, hour-glass	1	...	....	...	...	....
Stomatitis	2	...	....	1	...	....
Stricture, œsophagus	4	...	....	...	...	....
Stricture, rectum	...	...	....	1	...	....
Stricture, urethra	2	...	....	3	...	....
Strongyloides intestinalis	1	...	....	...	...	....
Subacidity	...	...	....	1	...	....
Subluxation, sacro-iliac	1	...	....	...	...	....
Synovitis	2	...	....	1	...	....
Synovitis, knee	1	...	....	...	...	....
Syphilis	131	2	1.5	34	2	5.9
Syphilis, cerebral	...	...	....	1	...	....
Syphilophobia	1	...	....	...	...	....
Syringomyelia	3	...	....	...	...	....
Tabes dorsalis	44	1	2.3	4	...	....
Tabo-paresis	1	...	....	...	...	....
Tænia saginata	1	...	....	1	...	....
Talipes equino-varus	1	...	....	...	...	....
Teleangiectasis	7	...	....	...	...	....
Teniasis	2	...	....	4	...	....
Tetanus	7	3	42.9	2	...	....
Thickened pleura	7	...	....	...	...	....
Thrombosis	6	...	....	3	...	....
Thrombosis, axillary	1	...	....	...	...	....
Thrombosis, cerebral	3	...	....	...	...	....
Thrombosis, femoral	...	...	....	1	...	....
Thrombosis, iliac	1	...	....	...	...	....
Thrombosis, venous	1	1	100.0	1	...	....
Tinea cruris	1	...	....	...	...	....
Tonsillitis	129	2	1.6	93	...	....
Torticollis	6	...	....	6	...	....
Tremor	1	...	....	2	...	....
Trichinosis	2	...	....	1	...	....
Tuberculosis, abscess	1	...	....	...	...	....
Tuberculosis, arthritis	3	...	....	1	...	....
Tuberculosis, bone	...	...	....	1	1	100.0
Tuberculosis, cæcum	...	...	....	1	...	....
Tuberculosis, clavicle	...	...	....	1	...	....
Tuberculosis, general	3	2	66.7	4	...	....
Tuberculosis, genito-urinary tract	1	1	100.0	...	...	....
Tuberculosis, glandular	3	...	....	3	...	....
Tuberculosis, hip joint	1	...	....	4	...	....
Tuberculosis, intestines	1	...	....	1	1	100.0
Tuberculosis, larynx	3	...	....	2	...	....
Tuberculosis, meningeal	20	14	70.0	13	10	76.9
Tuberculosis, mesenteric glands	1	...	....	...	...	....
Tuberculosis, miliary	4	3	75.0	2	2	100.0

TABLE 42. WHITE MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Tuberculosis, peritoneal	5	1	20.0	...	...	....
Tuberculosis, peritoneal, pleural	1	1	100.0	...	...	....
Tuberculosis, pleural	4	...	....	...	...	....
Tuberculosis, pleural, pericardial, meningeal	...	...	....	1	1	100.0
Tuberculosis, pleural and peritoneal	1	...	....	1	...	....
Tuberculosis, polyserositis	1	...	....	...	...	....
Tuberculosis, pulmonary	280	20	7.1	143	7	4.9
Tuberculosis, pulmonary and intestinal	3	2	66.7	...	...	....
Tuberculosis, pulmonary and laryngeal	5	...	....	...	...	....
Tuberculosis, pulmonary and meningeal	1	1	100.0	...	...	....
Tuberculosis, renal	2	1	50.0	...	...	....
Tuberculosis, sacro-iliac joint	2	...	....	1	...	....
Tuberculosis, spine	9	...	....	4	1	25.0
Tuberculosis, spleen	1	1	100.0	...	...	....
Tuberculosis, spondylitis	2	...	....	2	1	50.0
Tumor, abdominal	2	...	....	3	...	....
Tumor, bladder	...	...	....	1	...	....
Tumor, cauda equina	1	...	....	...	...	....
Tumor, cerebral	41	3	7.3	21	2	9.5
Tumor, colon	1	...	....	...	...	....
Tumor, kidney	4	...	....	...	...	....
Tumor, liver	3	...	....	1	...	....
Tumor, mediastinal	2	1	50.0	2	1	50.0
Tumor, pylorus	1	...	....	...	...	....
Tumor, retroperitoneal	1	...	....	...	...	....
Tumor, spinal cord	2	1	50.0	...	...	....
Tumor, testicle	2	...	..	...	...	....
Typhoid spine	5	...	...	1	...	....
Ulcer, duodenal	9	...	....	1	...	....
Ulcer, gastric	39	...	....	21	...	....
Ulcer, rectum	1	...	....	...	...	....
Uncinariasis	15	...	....	...	...	....
Uncinate gyrus attacks	1	...	....	...	...	....
Uræmia	2	2	100.0	3	3	100.0
Urethritis	25	...	....	2	...	....
Urticaria	3	...	....	1	...	....
Uveitis	...	...	....	1	...	....
Vaccination	6	...	....	...	...	....
Vaginitis	...	...	....	4	...	....
Varicella	1	...	....	2	...	....
Varicose veins	1	...	....	1	...	....
Vertigo	8	...	....	1	...	....
Vomiting, hysterical	1	...	....	...	...	....
Vomiting, pernicious	...	...	....	1	...	....
Vomiting, pregnancy	...	...	....	1	...	....
Wound, gunshot	...	...	....	1	...	....
Zeroderma pigmentosa	1	...	....	1	...	....
*Unclassified	91	21	23.1	37	6	16.2

* Includes cases of doubtful terminology.

TABLE 43. WHITE SURGICAL CASES.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abdominal pain	17	...	....	5	...	....
Aberrant thyroid	...	...	....	1	...	....
Abscess, abdominal	11	2	18.2	10	1	10.0
Abscess, alveolar	12	...	....	5	...	....
Abscess, antrum of Highmore	1	1	100.0	...	...	....
Abscess, arm	3	...	....	2	...	....
Abscess, axillary	14	1	7.1	1	...	....
Abscess, back	6	...	....	...	...	....
Abscess, breast	1	...	....	11	...	....
Abscess, buttocks	7	...	....	...	...	....
Abscess, cerebral	4	3	75.0	4	1	25.0
Abscess, cervical	9	1	11.1	3	...	....
Abscess, cheek	3	...	....	...	...	....
Abscess, chest wall	4	...	....	2	...	....
Abscess, elbow	2	...	....	...	...	....
Abscess, face	4	...	....	...	...	....
Abscess, foot	2	...	....	...	...	....
Abscess, groin	5	1	20.0	...	...	....
Abscess, iliac	1	...	....	...	...	....
Abscess, inguinal	...	...	....	1	...	....
Abscess, intermuscular	...	...	....	1	...	....
Abscess, intra-abdominal	4	2	50.0	1	...	....
Abscess, intracranial	3	1	33.3	...	...	....
Abscess, ischio-rectal	6	...	....	...	...	....
Abscess, jaw	4	...	....	...	...	....
Abscess, leg	17	2	11.8	11	1	9.1
Abscess, lip	1	...	....	...	...	....
Abscess, liver	18	5	27.7	...	...	....
Abscess, liver, amœbic	9	4	44.4	...	...	....
Abscess, lumbar	4	...	....	2	...	....
Abscess, lung	2	...	....	1	...	....
Abscess, mastoid	5	1	20.0	4	1	25.0
Abscess, mouth	1	...	....	...	...	....
Abscess, neck	22	...	....	6	...	....
Abscess, nose	1	...	....	...	...	....
Abscess, palmar	1	...	....	...	...	....
Abscess, pelvic	...	...	....	1	1	100.0
Abscess, perigastric	1	...	....	...	...	....
Abscess, perineal	8	...	....	...	...	....
Abscess, perinephritic	18	2	11.1	...	...	....
Abscess, periprostatic	1	1	100.0	...	...	....
Abscess, perirectal	53	...	....	8	...	....
Abscess, perirenal	2	...	....	...	...	....
Abscess, peritonsillar	10	...	....	3	...	....
Abscess, periurethral	14	1	7.1	...	...	....
Abscess, pharynx	1	...	....	...	...	....
Abscess, popliteal	3	...	....	1	...	....
Abscess, prepatellar bursa	...	...	....	1	...	....
Abscess, prostate	5	1	20.0	...	...	....
Abscess, psoas	2	...	....	4	...	....
Abscess, rectal	1	...	....	...	...	....
Abscess, retroperitoneal	3	...	....	...	...	....
Abscess, retropharyngeal	2	1	50.0	1	...	....
Abscess, sacro-iliac	...	...	....	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abscess, sacrum	...	...	....	1	...	....
Abscess, scalp	1	...	....	...	...	....
Abscess, scapula	1	...	....	...	...	....
Abscess, scrotum	7	...	....	...	...	....
Abscess, shin	1	...	....	...	...	....
Abscess, shoulder	1	...	....	...	...	....
Abscess, sinus, frontal	2	...	....	...	...	....
Abscess, space of Retzius	1	...	....	...	...	....
Abscess, spleen	...	...	....	1	...	....
Abscess, stitch	1	...	....	...	...	....
Abscess, subphrenic	5	...	....	...	...	....
Abscess, temporal	2	1	50.0	...	...	....
Abscess, thigh	25	...	....	2	...	....
Abscess, tonsillar	1	1	100.0	...	...	....
Abscess, trachea	1	...	....	...	...	....
Abscesses, multiple	4	...	....	3	1	33.3
Achlorhydria	1	...	....	...	...	....
Acromegaly	7	1	14.3	5	1	20.0
Actinomycosis	7	...	....	...	...	....
Actinomycosis, liver	...	...	....	1	...	....
Actinomycosis, ribs	1	...	....	...	...	....
Addison's disease	3	1	33.3	...	...	....
Adenitis, axillary	1	...	....	1	...	....
Adenitis, axillary, suppurative	2	...	....	1	...	....
Adenitis, cervical	...	...	....	2	...	....
Adenitis, cervical, inflammatory	...	...	....	1	...	....
Adenitis, cervical, suppurative	5	...	....	6	1	16.7
Adenitis, inguinal	5	...	....	2	...	....
Adenitis, inguinal, chancroidal	3	...	....	...	...	....
Adenitis, inguinal, suppurative	27	...	....	4	...	....
Adenitis, inguinal and iliac	1	...	....	...	...	....
Adenitis, submaxillary	1	...	....	1	...	....
Adeno-carcinoma	2	...	....	4	...	....
Adeno-carcinoma, cheek	1	...	....	...	...	....
Adeno-carcinoma, rectum	1	...	....	...	...	....
Adeno-fibroma, breast	...	...	....	2	...	....
Adenoids	8	...	....	6	...	....
Adenoma	...	...	....	5	...	....
Adenoma, thyroid	1	...	....	7	...	....
Adenomata, multiple	1	...	....	...	...	....
Adherent prepuce	1	...	....	...	...	....
Adhesion, peritoneal	2	...	....	...	...	....
Adhesions	4	...	....	11	...	....
Alcoholism	5	...	....	...	...	....
Amentia, infantile	1	...	....	1	...	....
Amputation, stump	10	...	....	3	...	....
Amputation, traumatic	7	2	28.6	...	...	....
Anæmia, pernicious	2	...	....	1	...	....
Anæmia, splenic	1	...	....	...	...	....
Aneurism	30	3	10.0	4	...	....
Aneurism, abdominal	1	...	....	...	...	....
Aneurism, aortic	1	...	....	...	...	....
Aneurism, arterio-venous	3	...	....	...	...	....
Aneurism, sciatic artery	1	1	100.0	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Aneurism, subclavian	...	...	....	1	...	....
Angina	3	...	....	...	...	....
Angina, Ludwig's	1	...	....	1	...	....
Angioma	3	...	....	2	...	....
Angioma, abdominal	1	...	....	...	...	....
Angioma, cheek	1	...	....	...	...	....
Angioma, chest wall	...	...	....	1	...	....
Angioma, eyelid	...	...	....	1	...	....
Angioma, lip	4	...	....	4	...	....
Angioma, neck	1	...	....	...	...	....
Angioma, scalp	1	...	....	...	...	....
Angioma, thigh	1	...	....	...	...	....
Angiomata, multiple	...	...	....	2	...	....
Angiosarcoma, rectum	...	...	....	1	...	....
Ankylosis	12	...	....	7	...	....
Ankylosis, elbow	1	...	....	...	...	....
Ankylosis, hip	1	...	....	...	...	....
Ankylosis, jaw	3	...	....	3	...	....
Ankylosis, knee	2	...	....	1	...	....
Ankylosis, shoulder	2	...	....	...	...	....
Aphonia, hysterical	...	...	....	1	...	....
Apoplexy, cerebral	2	2	100.0	3	1	33.3
Appendicitis	791	28	3.5	409	6	1.5
Arachnoiditis	1	...	....	...	...	....
Argyria	1	...	....	...	...	....
Arteriosclerosis	10	3	30.0	4	...	....
Arthritis	6	...	....	...	...	....
Arthritis deformans	16	...	....	8	...	....
Arthritis, elbow	3	...	....	...	...	....
Arthritis, foot, infectious	...	...	....	1	...	....
Arthritis, hip	5	...	....	6	...	....
Arthritis, hip, rheumatoid	1	...	....	...	...	....
Arthritis, hip, villous	1	...	....	...	...	....
Arthritis, infectious	43	...	....	50	2	4.0
Arthritis, knee	12	...	....	12	...	....
Arthritis, knee, infectious	2	...	....	3	...	....
Arthritis, knee, suppurative	6	...	....	...	...	....
Arthritis, knee, traumatic	2	...	....	1	...	....
Arthritis, knee, villous	6	...	....	1	...	....
Arthritis, metacarpophalangeal	3	...	....	...	...	....
Arthritis, shoulder	1	...	....	...	...	....
Arthritis, sternoclavicular joint	...	...	....	1	...	....
Arthritis, suppurative	1	...	....	...	...	....
Arthritis, tarsus	1	...	....	...	...	....
Arthritis, traumatic	5	...	....	...	...	....
Arthritis, villous	1	...	....	4	...	....
Arthritis, wrist	...	...	....	1	...	....
Arthritis, wrist, infectious	...	...	....	2	...	....
Arthropathy (Charcot)	1	...	....	...	...	....
Ascaris lumbricoides	...	...	....	1	...	....
Ascites	1	...	....	...	...	....
Asthma	...	...	....	1	...	....
Athetosis, double	1	...	....	...	...	....
Atresia, rectum	...	...	....	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Atresia, small intestines, congenital	1	...	....	...	...	....
Atrophy, progressive muscular	1	...	....	...	...	....
Bacteriuria	1	...	....	...	...	....
Blood transfusion	...	...	....	1	...	....
Bronchiectasis	...	...	....	3	...	....
Bronchitis	3	...	....	...	...	....
Burn	54	12	22.2	37	22	59.5
Burn, arm	1	1	100.0	...	...	....
Burn, carbolic acid	1	...	....	1	...	....
Burn, face and hands	2	...	....	...	...	....
Burn, hand	...	...	....	1	...	....
Burn, superficial	21	9	42.9	22	10	45.5
Bursitis	24	...	....	8	...	....
Bursitis, suppurative	1	...	....	1	...	....
Cachexia	...	...	....	1	...	....
Calculus, biliary	83	10	12.0	143	9	6.3
Calculus, prostatic	1	...	....	...	...	....
Calculus, renal	43	...	....	2	...	....
Calculus, submaxillary	2	...	....	...	...	....
Calculus, ureteral	16	...	....	...	...	....
Calculus, urethral	9	1	11.1	...	...	....
Calculus, vesical	62	2	3.2	2	...	....
Callus, foot	1	...	....	...	...	....
Cancrum oris	2	1	50.0	...	...	....
Carbuncle	34	...	....	6	...	....
Carcinoma, abdominal wall	1	...	....	...	...	....
Carcinoma, antrum	3	...	....	2	...	....
Carcinoma, appendix	1	...	....	...	...	....
Carcinoma, axilla	5	...	....	4	...	....
Carcinoma, bile duct	2	1	50.0	3	3	100.0
Carcinoma, bladder	30	10	33.3	1	...	....
Carcinoma, breast	2	1	50.0	248	14	5.6
Carcinoma, cæcum	8	1	12.5	...	...	....
Carcinoma, cervical glands	25	8	32.0	2	...	....
Carcinoma, cheek	5	...	....	...	...	....
Carcinoma, chest wall	...	...	....	10	...	....
Carcinoma, colon	5	3	60.0	3	1	33.3
Carcinoma, ear	1	...	....	...	...	....
Carcinoma, face	11	1	9.1	...	...	....
Carcinoma, fauces	1	...	....	...	...	....
Carcinoma, foot	1	...	....	1	...	....
Carcinoma, gall bladder	3	3	100.0	12	3	25.0
Carcinoma, groin	2	...	....	2	...	....
Carcinoma, gums	2	1	50.0	...	...	....
Carcinoma, hand	1	...	....	...	...	....
Carcinoma, humerus	...	...	....	1	...	....
Carcinoma, inferior maxilla	3	1	33.3	...	...	....
Carcinoma, inguinal gland	1	...	....	2	...	....
Carcinoma, intestines, multiple	9	4	44.4	4	2	50.0
Carcinoma, intra-abdominal	2	...	....	...	...	....
Carcinoma, jaw	3	...	....	1	...	....
Carcinoma, kidney	2	...	....	1	...	....
Carcinoma, larynx	4	1	25.0	...	...	....
Carcinoma, lip	23	2	8.7	2	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

	Males.			Females.		
Causes.	Ad-mitted.	Died.	Per cent.	Ad-mitted.	Died.	Per cent.
Carcinoma, lip and penis	1	...	....	...	...	....
Carcinoma, liver	9	2	22.2	3	1	33.3
Carcinoma, maxilla	1	...	....	...	...	....
Carcinoma, mouth	4	1	25.0	1	...	....
Carcinoma, neck glands	21	3	14.3	3	...	....
Carcinoma, neck and pharynx	1	...	....	...	...	....
Carcinoma, nose	1	1	100.0	...	...	....
Carcinoma, œsophagus	19	6	31.6	3	...	....
Carcinoma, orbit	1	1	100.0	...	...	....
Carcinoma, palate	2	1	50.0	...	...	....
Carcinoma, pancreas	15	3	20.0	7	2	28.6
Carcinoma, parotid	2	...	....	...	...	....
Carcinoma, pelvic glands	2	...	....	...	...	....
Carcinoma, penis	15	1	6.7	...	...	....
Carcinoma, pharynx	2	1	50.0	...	...	....
Carcinoma, prostate	83	9	10.8	...	...	....
Carcinoma, pylorus	4	2	50.0	2	1	50.0
Carcinoma, rectum	36	6	16.7	20	2	10.0
Carcinoma, retroperitoneal glands	1	...	....	...	...	....
Carcinoma, sacrum	1	...	....	...	...	....
Carcinoma, scalp	3	...	....	...	...	....
Carcinoma, scrotum	1	...	....	...	...	....
Carcinoma, sigmoid flexure	4	2	50.0	4	4	100.0
Carcinoma, spine	...	...	....	2	...	....
Carcinoma, stomach	69	10	14.5	30	5	16.7
Carcinoma, submaxillary gland	3	...	....	1	...	....
Carcinoma, superior maxilla	4	...	....	...	...	....
Carcinoma, temporal bone	1	...	....	...	...	....
Carcinoma, thyroid	1	...	....	5	...	....
Carcinoma, tongue	32	3	9.4	...	...	....
Carcinoma, tonsil	7	2	28.6	...	...	....
Carcinoma, uterus	...	...	....	1	...	....
Carcinoma, ventriculi	2	...	....	...	...	....
Carcinoma, vertebræ	3	...	....	1	...	....
Carcinosis, general	4	1	25.0	1	1	100.0
Carcinosis, peritoneal	2	...	....	...	...	....
Cardiospasm	...	...	....	1	...	....
Cellulitis	106	3	2.8	37	2	5.4
Cervical rib	1	...	....	1	...	....
Chancroid	4	...	....	...	...	....
Cholangitis	...	...	....	1	1	100.0
Cholecystitis	29	3	10.3	47	1	2.1
Cholesteatoma	...	...	....	1	1	100.0
Chondritis, typhoid	1	...	....	...	...	....
Cirrhosis, liver	11	5	45.5	6	2	33.3
Clavus, infected	1	...	....	...	...	....
Cleft palate	18	2	11.1	8	...	....
Club-foot	15	...	....	3	...	....
Coccygodynia	...	...	....	4	...	....
Colic, biliary	1	...	....	...	...	....
Colic, lead	3	...	....	...	...	....
Colic, renal	12	...	....	...	...	....
Colitis	6	1	16.7	4	...	....
Colitis, mucous	3	...	....	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Ad-mitted.	Died.	Per cent.	Ad-mitted.	Died.	Per cent.
Colitis, polypoid	4	1	25.0	...	...	....
Compression, spinal cord	...	...	....	1	...	....
Concussion, brain	14	1	7.1	...	...	....
Condylomata	2	...	....	1	...	....
Congested verumontanum	1	...	....	...	...	....
Constipation	6	...	....	3	...	....
Contracting, scar	...	...	....	1	...	....
Contracture, arm	...	...	....	1	...	....
Contracture, face	1	...	....	3	...	....
Contracture, hand	2	...	....	2	...	....
Contracture, plantar fascia	2	...	....	...	...	....
Contracture, tendons of forearm	1	...	....	...	...	....
Contractures	34	...	....	11	...	....
Contusion, abdomen	7	1	14.3	...	...	....
Contusion, arm	3	...	....	1	...	....
Contusion, back	4	...	....	1	...	....
Contusion, chest	1	...	....	...	...	....
Contusion, eye	1	...	....	...	...	....
Contusion, face	2	...	....	...	...	....
Contusion, foot	2	...	....	...	...	....
Contusion, head	12	...	....	...	...	....
Contusion, hip	2	...	....	...	...	....
Contusion, jaw	1	...	....	...	...	....
Contusion, kidney	4	...	....	...	...	....
Contusion, knee	2	...	....	1	...	....
Contusion, leg	7	...	....	...	...	....
Contusion, shoulder	3	...	....	...	...	....
Contusion, testicle	1	...	....	...	...	....
Contusion, thigh	1	...	....	...	...	....
Contusion, toe	1	...	....	...	...	....
Contusion, urethra	1	...	....	...	...	....
Contusion, vertebra	3	...	....	...	...	....
Contusions	34	...	....	6	...	....
Contusions, multiple	...	...	....	1	...	....
Cornu cutaneum	1	...	....	...	...	....
Coxa valga	1	...	....	...	...	....
Coxa vera	5	...	....	1	...	....
Curvature, spine, traumatic	1	...	....	...	...	....
Cyst, axilla	1	...	....	...	...	....
Cyst, bladder	1	...	....	...	...	....
Cyst, breast	1	...	....	45	...	....
Cyst, cerebellar	14	3	21.4	10	1	10.0
Cyst, chest wall	1	...	....	...	...	....
Cyst, dentigerous	...	...	....	2	...	....
Cyst, dermoid	2	...	....	3	...	....
Cyst, epididymis	2	...	....	...	...	....
Cyst, fibula	...	...	....	1	...	....
Cyst, humerus	1	...	....	1	...	....
Cyst, inferior maxilla	...	...	....	1	1	100.0
Cyst, kidney	1	...	....	...	...	....
Cyst, lip	1	...	....	...	...	....
Cyst, liver	...	...	....	1	...	....
Cyst, mesenteric	1	...	....	...	...	....
Cyst, neck	3	...	....	3	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Cyst, neurenteric	1	...	....	...	...	....
Cyst, ovarian	...	...	....	3	...	....
Cyst, pancreas	...	...	....	1	...	....
Cyst, scalp	...	...	....	1	...	....
Cyst, sebaceous	...	...	....	2	...	....
Cyst, thyroid	4	...	....	16	...	....
Cyst, thyroglossal	...	...	....	1	...	....
Cyst, kidney	5	1	20.0	...	...	....
Cystitis	61	2	3.3	2	...	....
Deafness	1	...	....	...	...	....
Deformity, face	1	...	....	2	...	....
Deformity, foot	2	...	....	1	...	....
Deformity, hand	...	...	....	1	...	....
Deformity, knee	1	...	....	...	...	....
Deformity, leg	1	...	....	...	...	....
Deformity, lip	1	...	....	...	...	....
Deformity, nose	8	...	....	2	...	....
Deformity, penis	1	...	....	...	...	....
Deformity, postoperative	1	...	....	...	...	....
Deformity, wrist	1	...	....	...	...	....
Delirium tremens	2	...	....	...	...	....
Dementia præcox	6	...	....	2	...	....
Dementia paralytica	1	...	....	...	...	....
Dementia, senile	1	...	....	...	...	....
Dermatitis	7	...	....	...	...	....
Dermatitis, blastomycetic	...	...	....	1	...	....
Dermatitis, iodoform	2	...	....	...	...	....
Dermatitis, leg	1	...	....	...	...	....
Diabetes mellitus	3	1	33.3	1	...	....
Dilatation, arteries	...	...	....	1	...	....
Dilatation, duodenum	...	...	....	2	...	....
Dilatation, stomach	...	...	....	1	...	....
Diphtheria	3	1	33.3	...	...	....
Dislocation	18	...	....	12	...	....
Dislocation, astragalus	1	...	....	...	...	....
Dislocation, clavicle	1	...	....	...	...	....
Dislocation, elbow	2	...	....	3	...	....
Dislocation, elbow, congenital	1	...	....	...	...	....
Dislocation, femur	1	1	100.0	...	...	....
Dislocation, femur, congenital	...	...	....	3	...	....
Dislocation, hip, congenital	3	...	....	9	...	....
Dislocation, humerus	2	...	....	1	...	....
Dislocation, interior cuneiform and scaphoid	1	...	....	...	...	....
Dislocation, knee	1	...	....	...	...	....
Dislocation, metacarpal bone	1	...	....	1	...	....
Dislocation, navicula	1	...	....	...	...	....
Dislocation, os calcis	1	...	....	...	...	....
Dislocation, os magnum	1	...	....	...	...	....
Dislocation, radius	4	...	....	...	...	....
Dislocation, radius and ulna	1	...	....	...	...	....
Dislocation, semilunar cartilage	1	...	....	...	...	....
Dislocation, shoulder	9	...	....	1	...	....
Dislocation, ulna	...	...	....	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

	Males.			Females.		
Causes.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Dislocation, vertebral	1	1	100.0	...	...	....
Diverticulitis	1	...	....	1	...	....
Diverticulum, bladder	2	...	....	...	...	....
Diverticulum, œsophagus	1	1	100.0	...	...	....
Diverticulum, urethral	1	...	....	...	...	....
Divided ulnar nerve	1	...	....	...	...	....
Division, tendon of thumb	1	...	....	...	...	....
Dupuytren's contracture	...	...	....	1	...	....
Dysentery, amœbic	14	3	21.4	...	...	....
Dysentery, chronic	1	1	100.0	...	...	....
Dysmenorrhœa	...	...	....	2	...	....
Dyspnœa	1	...	....	...	...	....
Dysuria	2	...	....	...	...	....
Ectropion	2	1	50.0	...	...	....
Eczema	3	...	....	1	...	....
Elephantiasis	3	...	....	...	...	....
Embolism, cerebral	1	1	100.0	...	...	....
Empyema	106	8	7.5	40	2	5.0
Encephalocele	...	...	....	3	...	....
Encysted stitch	1	...	....	...	...	....
Endocarditis	1	...	....	...	...	....
Endothelioma	4	...	....	...	...	....
Endothelioma, parotid	...	...	....	1	...	....
Enuresis, nocturnal	2	1	50.0	...	...	....
Enlarged aorta	...	...	....	1	...	....
Enteroptosis	2	...	....	13	1	7.7
Epididymitis	47	...	....	...	...	....
Epilepsy	105	2	1.9	34	...	....
Epiphyseal separation	1	...	....	...	...	....
Epiphysitis	11	1	9.1	3	...	....
Epistaxis	6	...	....	1	...	....
Epithelioma	91	5	5.5	13	...	....
Epithelioma, abdominal wall	...	...	....	1	...	....
Epithelioma, arm	1	...	....	...	...	....
Epithelioma, axilla	...	...	....	1	...	....
Epithelioma, eyelid	1	...	....	2	...	....
Epithelioma, face	12	...	....	3	...	....
Epithelioma, hand and nose	1	...	....	...	...	....
Epithelioma, leg	1	...	....	...	...	....
Epithelioma, lip	25	1	4.0	1	...	....
Epithelioma, nipple	...	...	....	1	...	....
Epithelioma, nose	2	...	....	2	...	....
Epithelioma, palate	1	...	....	1	...	....
Epithelioma, penis	4	1	25.0	...	...	....
Epithelioma, scalp	1	...	....	2	...	....
Epithelioma, skin over chest wall	1	...	....	...	...	....
Epithelioma, thigh	1	...	....	...	...	....
Epulis	2	...	....	3	...	....
Erysipelas	26	1	3.8	11	...	....
Ethmoiditis	5	...	....	...	...	....
Exophthalmos	1	...	....	2	...	....
Exostosis	18	...	....	2	...	....
Exostosis, femur	3	...	....	...	...	....
Exostosis, multiple	2	...	....	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Exostosis, os calcis	3	...	....	2	...	....
Exostosis, multiple	1	...	....	...	...	....
Exstrophy, bladder	1	...	....	...	...	....
Extravasation, urine	2	...	....	...	...	....
Facial tic	...	...	....	1	...	....
Fatty body in knee	1	...	....	1	...	....
Fever, cerebro-spinal	...	...	....	1	...	....
Fever, malarial	3	...	....	...	...	....
Fever, paratyphoid	1	...	....	1	...	....
Fever, scarlet	1	...	....	1	1	100.0
Fever, typhoid	24	12	50.0	6	3	50.0
Fever, typhoid (intestinal perforation)	12	11	91.7	2	1	50.0
Fibro-adenoma	...	...	....	1	...	....
Fibro-lipoma	5	...	....	1	...	....
Fibro-lipoma, groin	1	...	....	...	...	....
Fibroma	3	...	....	1	...	....
Fibroma, intracanalicular	...	...	....	1	...	....
Fibroma, molluscum	...	...	....	1	...	....
Fibroma, nose	1	1	100.0	...	...	....
Fibroma, palate	...	...	....	1	...	....
Fibro-sarcoma, spinal cord	1	1	100.0	...	...	....
Fissure in ano	35	...	....	9	...	....
Fistula, abdominal	1	...	....	...	...	....
Fistula in ano	136	1	0.7	12	...	....
Fistula, appendical	1	...	....	...	...	....
Fistula, arterio-venous	1	...	....	...	...	....
Fistula, biliary	2	...	....	3	1	33.3
Fistula, buccal	1	...	....	...	...	....
Fistula, fecal	9	...	....	5	...	....
Fistula, gastric	1	...	....	...	...	....
Fistula, intestinal	1	...	....	...	...	....
Fistula, perineal	9	1	11.1	...	...	....
Fistula, recto-urethral	5	1	20.0	...	...	....
Fistula, recto-vesical	2	...	....	...	...	....
Fistula, renal	2	...	....	1	...	....
Fistula, suprapubic	5	...	....	...	...	....
Fistula, scrotal	1	1	100.0	...	...	....
Fistula, urethral	13	...	....	...	...	....
Fistula, urinary	1	...	....	...	...	....
Fistula, vesical	1	...	....	...	...	....
Flat-foot	21	...	....	6	...	....
Floating cartilage	6	...	....	...	...	....
Foot drop	1	...	....	...	...	....
Foreign body in bronchus	4	1	25.0	...	...	....
Foreign body in cæcum	1	...	....	...	...	....
Foreign body in eye	1	...	....	...	...	....
Foreign body in face	1	...	....	...	...	....
Foreign body in foot	3	...	....	2	...	....
Foreign body in hand	...	...	....	2	...	....
Foreign body in knee	...	...	....	3	...	....
Foreign body in larynx	2	...	....	...	...	....
Foreign body in leg	2	...	....	1	...	....
Foreign body in œsophagus	5	2	40.0	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males. Admitted.	Males. Died.	Males. Per cent.	Females. Admitted.	Females. Died.	Females. Per cent.
Foreign body in os calcis	1	...	....	...	...	....
Foreign body in stomach	1	...	....	3	...	....
Foreign body in trachea	1	...	....	3	...	....
Fracture, acromion	1	...	....	...	...	....
Fracture, ankle	3	...	....	...	...	....
Fracture, astragalus	3	...	....	2	...	....
Fracture, clavicle	12	...	....	2	...	....
Fracture, coccyx	...	...	....	2	...	....
Fracture, Colles'	13	...	....	5	...	....
Fracture, cuboid	1	...	....	...	...	....
Fracture, elbow	9	1	11.1	2	...	....
Fracture, femur	115	3	2.6	41	1	2.4
Fracture, femur and skull	1	...	....	...	...	....
Fracture, fibula	14	...	....	3	...	....
Fracture, glenoid fossa	1	...	....	...	...	....
Fracture, hip	4	...	....	3	...	....
Fracture, humerus	47	...	....	19	1	5.3
Fracture, humerus and ulna	1	...	....	...	...	....
Fracture, ilium	2	...	....	...	...	....
Fracture, inferior maxilla	16	1	6.3	1	...	....
Fracture, jaw	5	...	....	...	...	....
Fracture, malleolus	1	...	....	...	...	....
Fracture, malleolus and fibula	1	...	....	...	...	....
Fracture, maxilla	1	...	....	1	...	....
Fracture, metacarpus	5	...	....	...	...	....
Fracture, metatarsus	9	...	....	2	...	....
Fracture, nasal bone	6	...	....	2	...	....
Fracture, olecranon	7	...	....	4	...	....
Fracture, os calcis	11	...	....	...	...	....
Fracture, patella	38	...	....	6	...	....
Fracture, pelvis	7	...	....	...	...	....
Fracture, phalanges	10	...	....	...	...	....
Fracture, Pott's	52	1	1.9	11	...	....
Fracture, radius	12	...	....	3	...	....
Fracture, radius and ulna	45	...	....	4	...	....
Fracture, rib	22	1	4.5	1	...	....
Fracture, scapula	3	...	....	...	...	....
Fracture, shoulder	...	...	....	1	...	....
Fracture, skull	103	18	17.5	18	5	27.7
Fracture, spine	3	...	....	...	...	....
Fracture, sternum	1	...	....	...	...	....
Fracture, superior maxilla	2	1	50.0	...	...	....
Fracture, thumb	2	...	....	...	...	....
Fracture, tibia	38	...	....	4	...	....
Fracture, tibia and fibula	100	2	2.0	9	...	....
Fracture, tibia and ribs	1	...	....	...	...	....
Fracture, ulna	7	...	....	1	...	....
Fracture, vertebra	17	1	5.9	2	...	....
Galactocele	...	...	....	1	...	....
Ganglion	2	...	....	4	...	....
Gangrene	21	2	9.5	8	1	12.5
Gastritis	5	...	....	1	...	....
Gastro-enteritis	8	1	12.5	5	...	....
Gastroptosis	1	...	....	2	1	50.0

TABLE 43. WHITE SURGICAL CASES—Continued.

	Males.			Females.		
Causes.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Genu valgum	12	...	....	1	...	....
Genu varum	5	...	....	2	...	....
Giant colon	...	...	....	1	1	100.0
Gigantism	1	...	....	...	...	....
Glioma	1	...	....	1	...	....
Glossitis	1	...	....	...	...	....
Goitre	8	...	....	41	1	2.4
Goitre, colloid	4	...	....	19	...	....
Goitre, cystic	...	...	....	3	...	....
Goitre, exophthalmic	39	3	7.7	156	9	5.8
Gonorrhœal adenitis, inguinal	4	...	....	1	...	....
Gonorrhœal arthritis	22	1	4.5	14	...	....
Gonorrhœal arthritis, ankle	1	...	....	...	...	....
Gonorrhœal arthritis, hip	1	...	....	...	...	....
Gonorrhœal arthritis, knee	11	...	....	5	...	....
Gonorrhœal arthritis, shoulder	...	...	....	1	...	....
Gonorrhœal arthritis, wrist	4	...	....	...	...	....
Gonorrhœal ophthalmia	1	...	....	...	...	....
Gonorrhœal peritonitis	...	...	....	1	...	....
Gonorrhœal salpingitis	...	...	....	1	...	....
Gonorrhœal urethritis	1	...	....	...	...	....
Granuloma	3	...	....	...	...	....
Growth, axilla (new)	1	...	....	...	...	....
Gumma	11	...	....	1	...	....
Gumma, back	...	...	....	1	...	....
Gumma, face	1	...	....	...	...	....
Gumma, frontal bone	2	...	....	...	...	....
Gumma, liver	1	...	....	...	...	....
Gumma, testicle	3	1	33.3	...	...	....
Gumma, toe	...	...	....	1	...	....
Hallux valgus	4	...	....	...	...	....
Hammer-toes	3	...	....	...	...	....
Harelip	17	2	11.8	13	...	....
Harelip and cleft palate	...	...	....	2	...	....
Headache	1	...	....	5	...	....
Hemangioma	2	...	....	2	...	....
Hematemesis	2	...	....	...	...	....
Hematoma	21	...	....	2	...	....
Hematoma, scalp	1	...	....	...	...	....
Hematomyelia	10	1	10.0	...	...	....
Hematoporphyrinuria	...	...	....	1	...	....
Hematuria	33	...	....	...	...	....
Hemianopsia	1	...	....	...	...	....
Hemiplegia	2	1	50.0	1	...	....
Hemophilia	2	...	....	...	...	....
Hemopneumothorax	1	...	....	...	...	....
Hemorrhage	27	4	14.8	7	...	....
Hemorrhage, cerebral	2	1	50.0	3	2	66.7
Hemorrhage, intestinal	1	...	....	...	...	....
Hemorrhage, pancreatic	1	1	100.0	...	...	....
Hemorrhage, postoperative	2	...	....	...	...	....
Hemorrhage, subdural	1	...	....	...	...	....
Hemorrhoids	227	...	....	30	...	....
Hepatitis	1	1	100.0	1	1	100.0

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Hernia, abdominal	1	...	....	...	...	....
Hernia cerebri	4	3	75.0	...	...	....
Hernia, epigastric	2	...	....	...	...	....
Hernia, femoral	16	...	....	21	1	4.8
Hernia, femoral, strangulated	8	4	50.0	12	2	16.7
Hernia, inguinal	648	5	0.8	35	...	....
Hernia, inguinal, double	28	...	....	1	...	....
Hernia, inguinal, left	27	...	....	3	...	....
Hernia, inguinal, right	80	...	....	6	...	....
Hernia, inguinal, strangulated	62	8	12.9	3	1	33.3
Hernia, postoperative	3	...	....	...	...	....
Hernia, umbilical	10	...	....	20	2	10.0
Hernia, umbilical, strangulated	2	1	50.0	6	3	50.0
Hernia, ventrical	10	...	....	20	2	10.0
Herpes	1	...	....	...	...	....
Hodgkin's disease	21	...	....	10	1	10.0
Horseshoe kidney	1	...	....	...	...	....
Hydrocele	120	1	1.7	2	...	....
Hydrocephalus	22	8	36.4	10	3	30.0
Hydronephrosis	5	...	....	1	...	....
Hydrosalpinx	...	...	....	1	...	....
Hyperacidity	1	1	100.0	...	...	....
Hypernephroma	4	2	50.0	1	...	....
Hyperthyroidism	...	...	....	2	...	....
Hypertrophied breast	4	...	....	...	...	....
Hypertrophied tonsils and adenoids	1	...	....	1	...	....
Hypertrophy, turbinates	3	...	....	3	...	....
Hypertrophy	10	1	10.0	6	...	....
Hypopituitarism	6	...	....	13	...	....
Hypospadias	20	...	....	...	...	....
Hypothyroidism	...	...	....	2	...	....
Hysteria	4	...	....	3	...	....
Hysterical hip	1	...	....	2	...	....
Hysterical spine	...	...	....	1	...	....
Icterus	1	1	100.0	...	...	....
Idiocy	2	...	....	1	...	....
Imbecility	...	...	....	1	...	....
Incontinence, feces	1	...	....	2	...	....
Incontinence, urine	7	...	....	...	...	....
Induration, penis	1	...	....	...	...	....
Infantilism	2	...	....	...	...	....
Infarct, septic	...	...	....	1	1	100.0
Infection, antrum	...	...	....	1	...	....
Infection, orbit	...	...	....	1	...	....
Inflammation, antrum of Highmore	1	...	....	...	...	....
Inflammation, intestinal	1	...	....	...	...	....
Inflammation, palate	1	...	....	...	...	....
Inflammation, ureteral orifice	1	...	....	...	...	....
Influenza	1	...	....	1	...	....
Ingrowing toe-nail	3	...	....	4	...	....
Injury, head	1	...	....	...	...	....
Insanity	1	...	....	1	...	....
Intestinal obstruction	40	11	27.5	13	5	38.5
Intestinal obstruction, strangulated	2	1	50.0	1	1	100.0

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Intestinal obstruction, volvulus	4	...	....	...	...	....
Intussusception	4	...	....	2	1	50.0
Irritable sphincter	1	...	....	...	...	....
Jaundice, catarrhal	4	1	25.0	1	...	....
Keloid	3	...	....	1	...	....
Kidney, floating	...	...	....	2	...	....
Kyphosis	1	...	....	...	...	....
Laceration	11	...	....	...	...	....
Laceration, hand	1	...	....	...	...	....
Laceration, lateral ligaments	1	...	....	...	...	....
Laceration, thigh	1	...	....	...	...	....
Lameness, intermittent	1	...	....	...	...	....
Laryngeal obstruction	2	...	....	...	...	....
Laryngitis	2	...	....	...	...	....
Leptomeningitis	1	...	....	...	...	....
Leukæmia	2	...	....	1	...	....
Leukæmia, spleno-myelogenous	1	...	....	...	...	....
Lipoma	12	...	....	8	...	....
Lipoma, abdominal wall	1	...	....	...	...	....
Lipoma, back	...	...	....	1	...	....
Lipoma, buttocks	1	...	....	...	...	....
Lipoma, groin	2	...	....	...	...	....
Lipoma, shoulder	...	...	....	3	...	....
Loose cartilage	1	...	....	...	...	....
Lordosis	1	...	....	...	...	....
Lues, cerebral	1	...	....	...	...	....
Lumbago	2	...	....	1	...	....
Lupus vulgaris	...	...	....	1	...	....
Lymphangioma	5	...	....	4	...	....
Lymphangitis	4	...	....	...	...	....
Lympho-sarcoma	3	1	33.3	...	...	....
Malformation, external genitalia, congenital	1	...	....	...	...	....
Malformation, anus, congenital	1	...	....	...	...	....
Malformation, thumb	1	...	....	...	...	....
Mastitis	...	...	....	17	1	5.9
Mastoiditis	23	2	8.7	19	1	5.3
Measles	1	...	....	...	...	....
Melano-sarcoma	1	...	....	...	...	....
Melena	1	...	....	...	...	....
Meningitis	18	10	55.6	1	1	100.0
Meningitis, cerebro-spinal	1	...	....	...	...	....
Meningocele	2	...	....	...	...	....
Meningo-encephalocele	...	...	....	1	...	....
Metatarsalgia	...	...	....	3	...	....
Microcephalia	...	...	....	1	...	....
Migraine	3	...	....	5	...	....
Mitral insufficiency	1	...	....	1	...	....
Morphinism	3	...	....	...	...	....
Myasthenia gravis	...	...	....	1	...	....
Myelitis	2	...	....	...	...	....
Myeloma	...	...	....	1	...	....
Myoma, hand	1	...	....	...	...	....
Myoma, uterus	...	...	....	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Myositis	3	...	....	1	...	....
Myxo-fibroma	1	...	....	...	...	....
Myxoma	...	...	....	10	...	....
Myxoma, breast	...	...	....	4	...	....
Myxo-sarcoma	2	...	....	8	...	....
Nasal spur	1	...	....	...	...	....
Necrosis	2	1	50.0	...	...	....
Necrosis, inferior maxilla	2	...	....	1	...	....
Necrosis, jaw	...	...	....	1	...	....
Necrosis, ribs	3	...	....	...	...	....
Necrosis, skull	2	...	....	...	...	....
Necrosis, superior maxilla	1	...	....	...	...	....
Necrosis, vertebræ	1	...	....	...	...	....
Neoplasm, cerebral	1	...	....	...	...	....
Nephritis	7	...	....	7	...	....
Nephrolithiasis	3	...	....	7	...	....
Nephroptosis	4	...	....	8	...	....
Neuralgia	14	...	....	17	...	....
Neuralgia, facial	59	1	1.7	82	1	1.2
Neuralgia, post-zoster	1	...	....	...	...	....
Neurasthenia	31	...	....	30	...	....
Neurasthenia, sexual	1	...	....	...	...	....
Neuritis	4	...	....	2	...	....
Neuritis, alcoholic	1	...	....	...	...	....
Neuritis, sciatic	1	...	....	...	...	....
Neuroma	3	...	....	1	...	....
Neuromata	...	...	....	1	...	....
Neurosis	1	...	....	1	...	....
Neurosis, gastric	5	...	....	1	...	....
Neurosis, traumatic	6	...	....	1	...	....
Nevus, pigmented	1	...	....	...	...	....
Non-erupted tooth	1	...	....	...	...	....
Obesity	1	...	....	...	...	....
Obstruction, œsophageal	1	...	....	...	...	....
Œdema	2	...	....	1	...	....
Œdema, arm	...	...	....	1	...	....
Œdema, cerebral	1	...	....	1	...	....
Œdema, foot	1	...	....	...	...	....
Œdema, leg	...	...	....	1	...	....
Onychia	...	...	....	1	...	....
Orchitis	8	...	....	...	...	....
Osteitis deformans	1	...	....	1	...	....
Osteoarthritis	11	...	....	2	...	....
Osteochondroma	2	...	....	1	...	....
Osteoma	6	...	....	2	...	....
Osteomyelitis	168	1	0.6	64	4	6.3
Osteomyelitis, astragalus	1	...	....	...	...	....
Osteomyelitis, femur	21	2	9.5	3	...	....
Osteomyelitis, fibula	2	...	....	1	...	....
Osteomyelitis, frontal bone	1	...	....	...	...	....
Osteomyelitis, humerus	9	...	....	5	...	....
Osteomyelitis, ilium	2	...	....	...	...	....
Osteomyelitis, inferior maxilla	2	...	....	...	...	....
Osteomyelitis, multiple	2	...	....	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Osteomyelitis, os calcis	...	...	....	1	...	....
Osteomyelitis, pelvis	3	...	....	...	...	....
Osteomyelitis, phalanges	4	...	....	1	...	....
Osteomyelitis, radius	2	...	....	...	...	....
Osteomyelitis, rib	5	...	....	1	...	....
Osteomyelitis, sternum	1	...	....	...	...	....
Osteomyelitis, tibia	19	...	....	8	...	....
Osteosarcoma, fibula	...	...	....	1	...	....
Otitis media	14	1	7.1	14	...	....
Oxycephaly	1	...	....	...	...	....
Pachymeningitis	2	...	....	3	...	....
Pain in side	1	...	....	1	...	....
Painful back	2	...	....	...	...	....
Painful breast	...	...	....	2	...	....
Painful heel	1	...	....	...	...	....
Painful leg	1	...	....	...	...	....
Painful micturition	1	...	....	...	...	....
Painful rib	...	...	....	1	...	....
Painful scar	1	...	....	1	...	....
Painful shoulder	1	...	....	...	...	....
Painful stitch	1	...	....	1	...	....
Painful wrist	1	...	....	1	...	....
Palsy	1	...	....	...	...	....
Palsy, cerebral	1	...	....	...	...	....
Palsy, infantile cerebral	1	1	100.0	2	...	....
Pancreatitis	6	1	16.7	1	...	....
Papilloma, bladder	19	...	....	3	...	....
Papilloma, mouth	...	...	....	1	...	....
Papilloma, peri-ureteral	...	...	....	1	...	....
Papilloma, prepuce	1	...	....	...	...	....
Papilloma, tongue	1	...	....	...	...	....
Papilloma, urethral roof	1	...	....	...	...	....
Papilloma, vocal cords	1	...	....	...	...	....
Paralysis	25	1	4.0	11	1	9.1
Paralysis, arm	1	...	....	...	...	....
Paralysis, brachial	...	...	....	1	...	....
Paralysis, circumflex nerve	...	...	....	1	...	....
Paralysis, hand	...	...	....	1	...	....
Paralysis, infantile	1	...	....	1	...	....
Paralysis, obstetrical	1	...	....	...	...	....
Paralysis, ulnar nerve	1	...	....	...	...	....
Paramyclonus multiplex	...	...	....	1	...	....
Paranoia	...	...	....	1	...	....
Paraphimosis	1	...	....	...	...	....
Paraplegia	2	...	....	...	...	....
Paraplegia, infantile	3	...	....	2	...	....
Paraplegia, spastic	1	...	....	...	...	....
Paratyphoid	1	...	....	...	...	....
Paresis	2	...	....	...	...	....
Parotitis	...	...	....	1	...	....
Pellagra	1	...	....	...	...	....
Perforation, intestinal	5	2	40.0	...	...	....
Pericarditis	1	1	100.0	...	...	....
Perichondritis	1	...	....	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Periostitis	11	...	....	3	...	....
Periostitis, femur	1	...	....	...	...	....
Periostitis, radius	2	...	....	...	...	....
Periostitis, superior maxilla	1	...	....	1	...	....
Periostitis, tibia	3	...	....	2	...	....
Periostitis, typhoid	1	...	....	...	...	....
Peritonitis	15	9	60.0	7	1	14.3
Peritonitis, traumatic	...	...	....	1	...	....
Perityphlitis	...	...	....	1	...	....
Pes cavus	...	...	....	1	...	....
Pharyngitis	1	...	....	...	...	....
Phimosis	12	...	....	...	...	....
Phlebitis	1	...	....	1	...	....
Pigmented mole	...	...	....	1	...	....
Pleurisy	4	...	....	2	...	....
Pleurisy, diaphragmatic	1	...	....	...	...	....
Pleurisy with effusion	3	...	....	...	...	....
Pneumonia	5	2	40.0	1	...	....
Pneumonia, broncho-	1	...	....	...	...	....
Poisoning, bichloride	1	...	....	...	...	....
Poisoning, cocaine	...	...	....	1	...	....
Poliomyelitis	4	...	....	10	...	....
Polycythæmia	...	...	....	1	...	....
Polyp, bladder	1	...	....	...	...	....
Polyp, nasal	2	...	....	1	...	....
Polyp, rectal	4	...	....	1	...	....
Porencephalitis	1	...	....	...	...	....
Pott's disease	1	1	100.0	...	...	....
Pregnancy	...	...	....	4	...	....
Proctitis	1	...	....	1	...	....
Prolapse, rectum	9	...	....	3	...	....
Prostate, enlarged	644	37	5.7	...	...	....
Prostate, hypertrophied	12	2	16.7	...	...	....
Prostatitis	68	...	....	...	...	....
Pruritus vulvæ	1	...	....	1	...	....
Psychasthenia	...	...	....	3	...	....
Psychoses, postoperative	...	...	....	1	...	....
Ptosis, congenital	1	...	....	...	...	....
Purpura, Henoch's	1	...	....	1	1	100.0
Pyæmia	1	1	100.0	1	...	....
Pyelitis	22	3	13.6	6	...	....
Pyelonephrosis	2	...	....	1	...	....
Pylorospasm	...	...	....	1	...	....
Pyonephrosis	9	1	11.1	...	...	....
Pyopneumothorax	2	1	50.0	...	...	....
Pyorrhœa	1	...	....	...	...	....
Pyrexia	...	...	....	1	...	....
Quinsy	...	...	....	1	...	....
Rachitis	1	...	....	2	...	....
Ranula	1	...	....	5	...	....
Recklinghausen's disease	1	...	....	1	...	....
Redundant colon	2	...	....	3	...	....
Redundant prepuce	1	...	....	...	...	....
Relaxed joints	6	...	....	3	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Relaxed vaginal outlet	...	...	....	3	...	....
Resected elbow	2	...	....	...	...	....
Retention, urine	4	1	25.0	...	...	....
Retroposition, uterus	...	...	....	2	...	....
Retroversion, uterus	...	...	....	1	...	....
Rheumatism	3	...	....	...	...	....
Rheumatism, chronic	1	...	....	...	...	....
Rhinitis	1	...	....	...	...	....
Rib, anomaly of	...	...	....	1	...	....
Rupture, biceps	1	1	100.0	...	...	....
Rupture, bladder	1	1	100.0	...	...	....
Rupture, brachial plexus	4	...	....	...	...	....
Rupture, capsule ankle-joints	1	...	....	...	...	....
Rupture, intestines	2	...	....	...	...	....
Rupture, kidney	2	...	....	1	...	....
Rupture, nerve trunks	1	...	....	...	...	....
Rupture, plantaris tendon	1	...	....	...	...	....
Rupture, sciatic nerve	1	...	....	...	...	....
Rupture, sphincter ani	1	...	....	...	...	....
Rupture, spleen, traumatic	2	...	....	...	...	....
Rupture, urethra	9	1	11.1	...	...	....
Rupture, vesical sphincter	1	...	....	...	...	....
Salpingitis	...	...	....	17	...	....
Sacro-iliac disease	1	...	....	...	...	....
Sarcoma, alveolar	1	1	100.0	...	...	....
Sarcoma, antrum	3	1	33.3	1	...	....
Sarcoma, arm	...	...	....	2	...	....
Sarcoma, axillary	1	...	....	1	...	....
Sarcoma, back	2	...	....	...	...	....
Sarcoma, breast	...	...	....	2	...	....
Sarcoma, buttocks	1	1	100.0	...	...	....
Sarcoma, cervical glands	5	1	20.0	1	1	100.0
Sarcoma, cheek	1	...	....	1	...	....
Sarcoma, chest wall	3	...	....	...	...	....
Sarcoma, ear	...	...	....	1	...	....
Sarcoma, femur	11	1	9.1	3	...	....
Sarcoma, fibula	1	...	....	1	...	....
Sarcoma, finger	1	...	....	...	...	....
Sarcoma, foot	1	...	....	2	...	....
Sarcoma, groin	2	...	....	...	...	....
Sarcoma, humerus	1	...	....	10	...	....
Sarcoma, ilium	4	...	....	...	...	....
Sarcoma, inferior maxilla	5	...	....	1	...	....
Sarcoma, inguinal glands	1	...	....	...	...	....
Sarcoma, intestines	1	1	100.0	...	...	....
Sarcoma, intraperitoneal	...	...	....	1	...	....
Sarcoma, jaw	2	...	....	1	...	....
Sarcoma, kidney	7	...	....	...	...	....
Sarcoma, knee	2	1	50.0	1	...	....
Sarcoma, leg	4	...	....	1	...	....
Sarcoma, lip	...	...	....	1	...	....
Sarcoma, mediastinal	1	...	....	...	...	....
Sarcoma, melanotic	...	...	....	1	...	....
Sarcoma, naso-pharynx	1	1	100.0	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Ad-mitted.	Died.	Per cent.	Ad-mitted.	Died.	Per cent.
Sarcoma, neck	7	1	14.3	...	...	....
Sarcoma, orbit	5	1	20.0	...	...	....
Sarcoma, ovary	...	...	....	2	2	100.0
Sarcoma, parotid	1	...	....	2	...	....
Sarcoma, pelvis	1	...	....	1	...	....
Sarcoma, pharynx	...	...	....	1	...	....
Sarcoma, prostate	1	...	....	...	...	....
Sarcoma, psoas muscle	1	...	....	...	...	....
Sarcoma, radius	...	...	....	1	...	....
Sarcoma, retroperitoneal	14	2	14.3	2	...	....
Sarcoma, scalp	...	...	....	1	...	....
Sarcoma, sciatic nerve	1	...	....	1	1	100.0
Sarcoma, scrotum	1	...	....	...	...	....
Sarcoma, skin	3	...	....	1	...	....
Sarcoma, skull	1	...	....	2	...	....
Sarcoma, shoulder	1	...	....	...	...	....
Sarcoma, stomach	...	...	....	1	...	....
Sarcoma, superior maxilla	4	2	50.0	1	...	....
Sarcoma, temporal bone	...	...	....	1	...	....
Sarcoma, testicle	6	3	50.0	...	...	....
Sarcoma, thigh	1	...	....	1	...	....
Sarcoma, thumb	2	...	....	...	...	....
Sarcoma, thyroid	2	...	....	1	1	100.0
Sarcoma, tibia	5	...	....	3	...	....
Sarcoma, tonsil	...	...	....	1	1	100.0
Sarcoma, vertebral	1	1	100.0	...	...	....
Sarcomatosis	1	...	....	1	...	....
Scar, breast	...	...	....	1	...	....
Scar, contracted	6	...	....	4	...	....
Scar, painful	4	...	....	5	...	....
Schimmelbusch's disease	...	...	....	1	...	....
Sciatica	8	...	....	6	...	....
Sclerosis	1	...	....	1	...	....
Scoliosis	6	...	....	3	...	....
Senile breast	...	...	....	1	...	....
Separation of epiphyses	20	...	....	7	...	....
Septicæmia	6	6	100.0	4	3	75.0
Sinus, abdominal	5	...	....	2	...	....
Sinus of amputation stump	...	...	....	1	...	....
Sinus following appendectomy	4	...	....	...	...	....
Sinus, arm	...	...	....	2	...	....
Sinus, axillary	1	...	....	...	...	....
Sinus, back	2	...	....	...	...	....
Sinus, buccal	1	...	....	...	...	....
Sinus, buttocks	1	...	....	...	...	....
Sinus, cervical	...	...	....	1	...	....
Sinus, chest	...	...	....	1	...	....
Sinus, flank	...	...	....	1	...	....
Sinus, foot	3	...	....	...	...	....
Sinus, groin	1	...	....	1	...	....
Sinus, jaw	1	...	....	...	...	....
Sinus, leg	1	...	....	...	...	....
Sinus, lumbar region	2	...	....	...	...	....
Sinus, neck	4	...	....	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Sinus, perineal	3	...	....	...	...	....
Sinus, pilonidal	12	...	....	2	...	....
Sinus, shoulder	1	...	....	1	...	....
Sinus, supra-pubic	3	...	....	...	...	....
Sinus, thigh	3	...	....	1	...	....
Sinus, urethral	1	...	....	...	...	....
Sinuses, multiple	2	...	....	...	...	....
Sinusitis	6	1	16.7	2	...	....
Skin, grafting	2	...	....	...	...	....
Slough, dorsum of foot	...	...	....	1	...	....
Snake bite	1	...	....	...	...	....
Spasm of glottis	1	...	....	1	...	....
Spermatocele	6	...	....	...	...	....
Spina bifida	1	1	100.0	3	2	66.7
Splenomegaly	2	...	....	...	...	....
Spondylitis	12	...	....	2	...	....
Spondylitis deformans	1	...	....	...	...	....
Spondylitis, post-typhoid	...	...	....	2	...	....
Spondylolisthesis	...	...	....	1	...	....
Sprain, ankle	4	...	....	4	...	....
Sprain, back	4	...	....	1	...	....
Sprain, knee	4	...	....	...	...	....
Sprain, wrist	3	...	....	1	...	....
Stenosis	1	1	100.0	...	...	....
Stenosis, pyloric	5	...	....	2	1	50.0
Stomach, hour-glass	2	...	....	...	...	....
Stomatitis	1	...	....	...	...	....
Strain, abdomen	1	...	....	...	...	....
Strain, muscular	1	...	....	...	...	....
Stricture, anus	1	...	....	...	...	....
Stricture, bile duct	1	...	....	...	...	....
Stricture, duodenum	1	1	100.0	1	...	....
Stricture, larynx	1	...	....	1	...	....
Stricture, œsophagus	9	...	....	1	...	....
Stricture, pylorus	10	2	20.0	...	...	....
Stricture, rectum	12	3	25.0	3	...	....
Stricture, ureter	2	...	....	...	...	....
Stricture, urethra	64	3	4.7	...	...	....
Subluxation, clavicle	1	...	....	...	...	....
Subluxation, joint	1	...	....	1	...	....
Subluxation, sacro-iliac	1	...	....	...	...	....
Subluxation, vertebra	1	...	....	...	...	....
Syndrome, polyglandular	1	...	....	1	...	....
Synovitis	5	...	....	2	...	....
Synovitis, knee	2	...	....	1	...	....
Syphilis	37	1	2.7	7	...	....
Syphilis, congenital	...	...	....	1	...	....
Syphilis, sternum	1	...	....	...	...	....
Syphilitic adenitis, cervical	...	...	....	1	...	....
Syphilitic arthritis, elbow	1	...	....	...	...	....
Syphilitic arthritis, knee	1	...	....	...	...	....
Syphilitic paraplegia	1	...	....	...	...	....
Syphilitic ulcer, arm	...	...	....	1	...	....
Syphilitic ulcer, leg	4	...	....	2	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Syringomyelia	1	...	....	...	...	....
Tabes dorsalis	16	...	....	1	...	....
Talipes equino-varus	11	1	9.1	11	...	....
Tender cartilages	...	...	....	1	...	....
Tenosynovitis	6	...	....	2	...	....
Tetanus	9	5	55.6	1	...	....
Thrombo-phlebitis	1	...	....	...	...	....
Thrombosis	8	2	25.0	3	1	33.3
Thrombosis, femoral vein	1	1	100.0	...	...	....
Thyroiditis	1	...	....	...	...	....
Thyroid, enlarged	1	...	....	1	...	....
Tinnitus aurium	2	...	....	...	...	....
Tonsillitis	27	...	....	26	2	7.7
Tonsils, enlarged	47	...	....	51	...	....
Torticollis	19	...	....	10	...	....
Transfusion, blood	1	...	....	...	...	....
Tubercle, cerebellar	3	2	66.7	...	...	....
Tuberculosis, abdominal wall	1	...	....	...	...	....
Tuberculosis, ankle	1	...	....	...	...	....
Tuberculosis, astragalus	1	...	....	...	...	....
Tuberculosis, bladder	6	...	....	...	...	....
Tuberculosis, breast	...	...	....	1	...	....
Tuberculosis, cæcum	...	...	....	1	...	....
Tuberculosis, cutis	3	...	....	...	...	....
Tuberculosis, elbow	...	...	....	1	...	....
Tuberculosis, epididymis	18	...	....	...	...	....
Tuberculosis, foot	1	...	....	...	...	....
Tuberculosis, genito-urinary tract	3	...	....	...	...	....
Tuberculosis, groin	1	...	....	...	...	....
Tuberculosis, hand, tendon sheaths	1	...	....	...	...	....
Tuberculosis, hip	8	...	....	3	...	....
Tuberculosis, humerus	...	...	....	1	...	....
Tuberculosis, kidney	20	1	5.0	2	...	....
Tuberculosis, larynx	4	1	25.0	...	...	....
Tuberculosis, liver	1	...	...	....	...	....
Tuberculosis, miliary general	1	1	100.0	...	...	....
Tuberculosis, neck	1	...	....	...	...	....
Tuberculosis, os magnum	1	...	....	...	...	....
Tuberculosis, pelvis	...	...	....	3	...	....
Tuberculosis, prostate	4	...	....	...	...	....
Tuberculosis, pulmonary	7	...	....	2	...	....
Tuberculosis, rectum	...	...	....	1	...	....
Tuberculosis, ribs	4	...	....	5	...	....
Tuberculosis, ribs and sternum	1	...	....	1	...	....
Tuberculosis, sacro-iliac	6	...	....	3	...	....
Tuberculosis, shoulder	1	...	....	...	...	....
Tuberculosis, skin	1	...	....	1	...	....
Tuberculosis, sternum	2	...	....	...	...	....
Tuberculosis, tarsus	1	...	....	1	...	....
Tuberculosis, tendon sheaths	2	...	....	...	...	....
Tuberculosis, testicle	1	...	....	...	...	....
Tuberculosis, tibia	...	...	....	1	...	....
Tuberculosis, trochanter	1	...	....	1	...	....
Tuberculosis, vas deferens	1	...	....	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Tuberculosis, vertebræ	82	4	4.9	41	2	4.9
Tuberculosis, vulva	...	...	....	1	...	....
Tuberculosis, wrist	1	...	....	...	...	....
Tuberculous abscess, cervical	1	...	....	...	...	....
Tuberculous adenitis, axillary	5	...	....	6	...	....
Tuberculous adenitis, cervical	64	...	....	67	1	1.5
Tuberculous adenitis, inguinal	10	...	....	3	...	....
Tuberculosis arthritis	76	2	2.6	37	...	....
Tuberculous arthritis, ankle	10	...	....	3	...	....
Tuberculous arthritis, elbow	7	...	....	4	...	....
Tuberculous arthritis, hip	45	1	2.2	31	2	6.5
Tuberculous arthritis, knee	28	...	....	15	...	....
Tuberculous arthritis, metacarpo-phalangeal	1	...	....	...	...	....
Tuberculous arthritis, sacro-iliac joints	6	1	16.7	1	...	....
Tuberculous arthritis, shoulder	6	...	....	...	...	....
Tuberculous arthritis, tarsus	...	...	....	1	...	....
Tuberculous arthritis, wrist	5	...	....	...	...	....
Tuberculous cystitis	2	...	....	...	...	....
Tuberculous meningitis	4	3	75.0	3	3	100.0
Tuberculous peritonitis	2	1	50.0	1	...	....
Tuberculous pleurisy	1	...	....	1	...	....
Tuberculous sinus	...	...	....	1	...	....
Tuberculous sinus, hip	1	...	....	...	...	....
Tuberculous tenosynovitis	...	...	....	1	...	....
Tuberculous ulcer, foot	1	...	....	...	...	....
Tumor, abdominal	8	...	....	7	1	14.3
Tumor, bladder	8	...	....	...	...	....
Tumor, bone	1	...	....	1	...	....
Tumor, brain	153	35	22.9	82	17	20.7
Tumor, breast	1	...	....	2	...	....
Tumor, buttocks	...	...	....	1	...	....
Tumor, epididymis	1	...	....	...	...	....
Tumor, face	1	...	....	...	...	....
Tumor, foot	1	...	....	...	...	....
Tumor, humerus	1	...	....	...	...	....
Tumor, hypophysis	17	3	17.6	6	...	....
Tumor, kidney	1	1	100.0	1	...	....
Tumor, mediastinal	1	...	....	...	...	....
Tumor, neck	2	...	....	...	...	....
Tumor, palate	1	...	....	...	...	....
Tumor, parotid	9	...	....	6	...	....
Tumor, pons	1	...	....	1	...	....
Tumor, popliteal nerve	1	...	....	4	...	....
Tumor, prostate	1	...	....	...	...	....
Tumor, scalp	...	...	....	1	...	....
Tumor, sigmoid flexure	1	...	....	...	...	....
Tumor, spinal cord	13	...	....	7	...	....
Tumor, testicle	3	...	....	...	...	....
Tumor, thyroid	1	1	100.0	3	...	....
Tumor, tonsil	2	...	....	...	...	....
Tumor, trachea	...	...	....	1	...	....
Tumor, uterus	...	...	....	1	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Turbinates, enlarged	2	...	....	...	...	....
Typhoid spine	1	...	....	...	...	....
Ulcer, abdominal wall	1	...	....	...	...	....
Ulcer, arm	1	...	....	...	...	....
Ulcer, back	...	...	....	1	...	....
Ulcer, bladder	1	...	....	...	...	....
Ulcer, cheek	2	...	....	...	...	....
Ulcer, duodenal	9	3	33.3	3	1	33.3
Ulcer, face	1	...	....	...	...	....
Ulcer, finger	2	...	....	...	...	....
Ulcer, foot	6	...	....	...	...	....
Ulcer, gastric	14	3	21.4	6	2	33.3
Ulcer, hand	1	...	....	...	...	....
Ulcer, heel, with foot	3	...	....	...	...	....
Ulcer, leg	17	...	....	4	...	....
Ulcer, lip	1	...	....	...	...	....
Ulcer, mouth	1	...	....	...	...	....
Ulcer, nose	1	...	....	...	...	....
Ulcer, penis	1	...	....	...	...	....
Ulcer, pylorus	1	...	....	1	...	....
Ulcer, rectum	4	...	....	2	...	....
Ulcer, scar of old burn	1	...	....	...	...	....
Ulcer, thigh	2	...	....	...	...	....
Ulcer, tongue	1	...	....	...	...	....
Ulcer, tonsil	1	...	....	...	...	....
Ulcer, urethra	1	...	....	...	...	....
Ulcer, varicose	4	...	....	2	...	....
Undescended testicle	6	...	....	...	...	....
Uræmia	3	2	66.7	...	...	....
Ureter, double	1	...	....	...	...	....
Urethral defect	1	...	....	...	...	....
Urethritis	32	...	....	...	...	....
Varicocele	105	...	....	...	...	....
Varicose veins	60	...	....	22	...	....
Vera montanitis	3	...	....	...	...	....
Vertigo	1	...	....	1	...	....
Vesiculitis	1	...	....	...	...	....
Volvulus	10	1	10.0	...	...	....
Vomiting	1	...	....	...	...	....
Wart	1	...	....	...	...	....
Web fingers	1	...	....	...	...	....
Wound, abdomen	1	...	....	...	...	....
Wound, abdomen, gunshot	...	...	....	1	...	....
Wound, abdomen, stab	1	...	....	...	...	....
Wound, ankle, lacerated	1	...	....	...	...	....
Wound, ankle, superficial	1	...	....	...	...	....
Wound, anus	1	...	....	...	...	....
Wound, arm, granulating	1	...	....	...	...	....
Wound, arm, incised	1	...	....	...	...	....
Wound, arm, infected	4	...	....	...	...	....
Wound, contracted	1	...	....	...	...	....
Wound, contused	5	...	....	2	...	....
Wound, eye	1	...	....	...	...	....
Wound, eye, gunshot	1	...	....	...	...	....

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Wound, face, granulating	1	...	....	...	...	....
Wound, face, gunshot	1	...	....	...	...	....
Wound, face, lacerated	1	...	....	...	...	....
Wound, finger, infected	1	...	....	...	...	....
Wound, foot, gunshot	2	...	....	...	...	....
Wound, foot, infected	1	...	....	1	1	100.0
Wounds, granulating	18	...	....	6	...	....
Wounds, gunshot	57	10	17.5	10	...	....
Wound, hand, infected	2	...	....	1	...	....
Wound, hand, lacerated	1	...	....	...	...	....
Wound, hand and arm, lacerated	1	...	....	...	...	....
Wound, incised	20	...	....	3	...	....
Wounds, infected	70	5	7.1	18	1	5.6
Wounds, lacerated	45	3	6.7	8	...	....
Wound, leg, gunshot	1	...	....	...	...	....
Wound, leg, infected	3	1	33.3	...	...	....
Wound, lip, incised	1	...	....	...	...	....
Wound, neck, granulating	1	...	....	...	...	....
Wound, perineum, lacerated	1	...	....	...	...	....
Wound, punctured	6	...	....	2	...	....
Wound, scalp	10	...	....	6	...	....
Wound, scalp, lacerated	1	1	100.0	1	...	....
Wound, skull, gunshot	2	...	....	...	...	....
Wound, spine, gunshot	1	...	....	...	...	....
Wounds, stab	13	...	....	1	...	....
Wound, thigh	1	...	....	...	...	....
Wound, throat, incised	1	...	....	...	...	....
Wry neck	...	...	....	1	...	....
X-ray burn	...	...	....	1	...	....
*Unclassified	3	...	....	7	...	....
Eye and ear cases:						
Abscess, epidural	1	...	....	...	...	....
Abscess, mastoid	1	...	....	1	...	....
Atrophy, optic	...	...	....	3	...	....
Blindness	2	...	....	...	...	....
Burn of eye	1	...	....	...	...	....
Cataract	40	...	....	32	...	....
Cholesteatoma	...	...	....	1	...	....
Choriditis	1	...	....	...	...	....
Conjunctivitis	2	...	....	4	...	....
Contusion, eye	2	...	....	...	...	....
Corneal opacity	1	...	....	...	...	....
Cyst, eyelid	...	...	....	1	...	....
Cyst, lachrymal gland	1	...	....	...	...	....
Dacryocystitis	1	...	....	...	...	....
Detachment, retina	1	...	....	...	...	....
Ectropion, upper lid	1	...	....	...	...	....
Endothelioma, lachrymal gland	1	...	....	...	...	....
Enucleation, eye	3	...	....	2	...	....
Foreign body in eye	21	...	....	...	...	....
Glaucoma	9	...	....	4	...	....
Hemorrhage after tonsillotomy	1	...	....	...	...	....
Hernia, iris	2	...	....	...	...	....

* Includes cases of doubtful terminology.

TABLE 43. WHITE SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Infection, orbit	...	...	....	2	...	....
Inflammation, middle ear	1	...	....	1	...	....
Intra-ocular neoplasm	1	...	....	...	...	....
Irido-cyclitis	27	...	....	4	...	....
Irido-dialysis	1	...	....	...	...	....
Iritis	6	...	....	2	...	....
Irritation, sympathetic	1	...	....	...	...	....
Keratitis	6	...	....	...	...	....
Keratocele	2	...	....	...	...	....
Laceration, eye	1	...	....	...	...	....
Mastoiditis	6	...	....	3	...	....
Metal in vitreous	3	...	....	...	...	....
Myopia	1	...	....	...	...	....
Occlusion, pupil	3	...	....	1	...	....
Opacity, corneal	1	...	....	...	...	....
Ophthalmia	1	...	....	...	...	....
Ophthalmia, sympathetic	2	...	....	...	...	....
Otitis media	13	2	15.4	7	...	....
Panophthalmitis	18	...	....	2	...	....
Phthisis bulbi	1	...	....	...	...	....
Ptosis	1	...	....	...	...	....
Retinitis	3	...	....	...	...	....
Rodent ulcer, cornea	3	...	....	...	...	....
Rupture, anterior capsule of lens	2	...	....	...	...	....
Rupture, eyeball	1	...	....	...	...	....
Rupture, iris	1	...	....	...	...	....
Sarcoma, choroid	3	...	....	1	...	....
Sclerosis, traumatic	1	...	....	...	...	....
Separation, retina	1	...	....	...	...	....
Staphyloma, cornea	1	...	....	...	...	....
Steel in vitreous	1	...	....	...	...	....
Stenosis, lachrymal duct	...	...	....	1	...	....
Strabismus	4	...	....	5	...	....
Symblepharon	2	...	....	...	...	....
Tinnitus	1	...	....	...	...	....
Trachoma	2	...	....	1	...	....
Ulcer, cornea	1	...	....	...	...	....
Uveitis	2	...	....	1	...	....
Wound, cornea	3	...	....	...	...	....
Wound, eyeball	7	...	....	1	...	....
Unclassified eye and ear cases	5	...	....	...	...	....

TABLE 44. WHITE GYNECOLOGICAL CASES.

Causes.	Admitted.	Died.	Per cent.
Abdominal pain	55	...	....
Abdominal trouble, obscure	1	1	100.0
Abnormal mobility of synchondrosis	1	...	....
Abortion	10	...	....
Abortion, incomplete	1	...	....
Abortion, infected	1	...	....
Abortion, threatened	10	...	....
Abortion, tubal	2	...	....
Abscess, abdominal	14	2	14.3
Abscess, broad ligament	3	...	....

TABLE 44. WHITE GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Abscess, ischio-rectal	5	...	....
Abscess, kidney	2	...	....
Abscess, ovarian	4	...	....
Abscess, pelvic	94	2	2.1
Abscess, perinephritic	2	1	50.0
Abscess, perirenal	1	...	....
Abscess, periurethral	1	...	....
Abscess, postoperative	1	...	....
Abscess, recto-vaginal septum	1	...	....
Abscess, renal	3	2	66.7
Abscess, suburethral	1	...	....
Abscess, tubo-ovarian	20	2	10.0
Abscess, uterus	1	...	....
Abscess, vulvo-vaginal glands	22	...	....
Abscess, uterus and vagina	1	...	....
Adenitis, inguinal	6	...	....
Adeno-myoma	3	1	33.3
Adeno-carcinoma, uterus	5	...	....
Adherent clitoris	2	...	....
Adhesions, intestinal	10	...	....
Adhesions, omental	2	...	....
Adhesions, pelvic	4	...	....
Adhesions, peritoneal	2	...	....
Adhesions, postoperative	56	2	3.6
Adiposis	1	...	....
Amenorrhœa	10	...	....
Anemia	2	...	....
Angioma	1	...	....
Appendicitis	216	2	0.9
Appendix, abscess	3	...	....
Appendix, adherent	6	...	....
Arthritis deformans	2	...	....
Ascites	4	...	....
Atresia	3	...	....
Atresia, uterine canal	1	...	....
Atresia, vagina	1	1	100.0
Bacilluria	1	...	....
Calculus, biliary	31	2	6.5
Calculus, renal	21	1	4.8
Calculus, ureteral	5	...	....
Calculus, vesical	3	...	....
Carcinoma, bladder	6	2	33.3
Carcinoma, breast	2	...	....
Carcinoma, clitoris	4	...	....
Carcinoma, cœcum	2	...	....
Carcinoma, colon	2	...	....
Carcinoma, Fallopian tubes	1	...	....
Carcinoma, gall bladder	1	...	....
Carcinoma, inguinal glands	1	...	....
Carcinoma, intestines	2	...	....
Carcinoma, kidney	1	...	....
Carcinoma, liver	3	1	33.3
Carcinoma, ovary	49	9	18.4
Carcinoma, pelvic glands	1	...	....
Carcinoma, pelvis	13	...	....
Carcinoma, pylorus	1	1	100.0

TABLE 44. WHITE GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Carcinoma, rectum	10	1	10.0
Carcinoma, sigmoid flexure	4	1	25.0
Carcinoma, small bowel	1	...	....
Carcinoma, stomach	3	1	33.3
Carcinoma, urethra	1	...	....
Carcinoma, uterus, body	6	1	16.7
Carcinoma, uterus, body and cervix	1	1	100.0
Carcinoma, uterus, cervix	201	24	11.9
Carcinoma, uterus, fundus	31	...	....
Carcinoma, vagina	20	...	....
Carcinoma; vulva	3	...	....
Carcinosis, general	4	1	25.0
Carcinosis, general with ascites	1	...	....
Carcinosis, peritoneal	2	...	....
Caruncle, urethral	22	1	4.5
Cellulitis	12	...	....
Cervicitis	2	...	....
Cholelithiasis	5	...	....
Cholecystitis	3	...	....
Chorio-epithelioma, uterus	1	...	....
Cirrhosis, liver	2	...	....
Coccygodynia	4	...	....
Colic, intestinal	2	...	....
Colic, renal	1	...	....
Colitis, mucous	1	...	....
Complete tear, recto-vaginal septum	34	1	2.9
Condylomata	1	...	....
Condylomata, vulva	1	...	....
Congenital absence of cervix	1	...	....
Constipation	4	...	....
Contusion, coccyx	1	...	....
Cribriform hymen	1	...	....
Cyst, abdominal	1	...	....
Cyst, Bartholin's glands	5	...	....
Cyst, corpus luteum	5	...	....
Cyst, ovarian	158	7	4.4
Cyst, ovarian, Graafian follicle	15	1	6.7
Cyst, ovarian, infected	2	...	....
Cyst, ovarian, intraligamentary	4	...	....
Cyst, ovarian, parovarian	1	...	....
Cyst, parovarian	28	...	....
Cyst, perineal	1	...	....
Cyst, retroperitoneal	1	...	....
Cyst, tubo-ovarian	1	...	....
Cyst, vaginal	1	...	....
Cystic kidney	1	...	....
Cystic ovary	1	...	....
Cystitis	132	...	....
Cystitis, ulcerative	2	1	50.0
Cystocele	14	...	....
Deciduoma malignum	2	1	50.0
Descensus uteri	14	...	....
Diabetes mellitus	2	...	....
Diastasis, rectal muscles	2	...	....
Dilated veins	1	...	....
Dislocation, ureter	1	...	....

TABLE 44. WHITE GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Dysmenorrhœa	294	...	....
Dyspareunia	2	...	....
Dysuria	1	...	....
Eczema	1	...	....
Elongated cervix	2	...	....
Emphysema	1	...	....
Endocervicitis	13	...	....
Endometritis	5	...	....
Enlarged floating spleen	1	...	....
Enteroptosis	3	...	....
Enuresis	3	...	....
Epilepsy	2	...	....
Epithelioma	1	...	....
Epithelioma, thigh	1	...	....
Epithelioma, vulva	4	...	....
Erosion, cervix	3	...	....
Eversion, rectal mucosa	1	...	....
Examination, cystoscopic	1	...	....
Fecal impaction	1	...	....
Fever, typhoid	4	...	....
Fibroid, labium majus	1	...	....
Fibroid, uterus	2	...	....
Fibroma, ovary	5	...	....
Fissure in ano	5	...	....
Fistula, abdominal and recto-vaginal	1	1	100.0
Fistula in ano	13	...	....
Fistula, biliary	1	...	....
Fistula, fecal	1	...	....
Fistula, urethro-vesico-vaginal	2	1	50.0
Fistula, recto-cervical	1	...	....
Fistula, recto-vaginal	6	...	....
Fistula, recto-vesico-vaginal	1	...	....
Fistula, uretero-abdominal	1	...	....
Fistula, uretero-vaginal	2	...	....
Fistula, vesico-abdominal	2	...	....
Fistula, vesico-urethro-vaginal	2	1	50.0
Fistula, vesico-vaginal	34	1	2.9
Fracture, coccyx	1	...	....
Gastroptosis	1	...	....
Gonorrhœa	2	...	....
Gonorrhœal peritonitis	1	...	....
Granuloma, urethra	1	...	....
Gumma, liver	2	...	....
Hematocele	2	...	....
Hematokolpos	1	...	....
Hematoma	3	...	....
Hematoma, ovary	1	...	....
Hematoma, pelvic	2	...	....
Hematometra	1	...	....
Hematosalpinx	2	...	....
Hematuria	19	...	....
Hemorrhage	1	...	....
Hemorrhage, postoperative	1	...	....
Hemorrhage, uterine	48	...	....
Hemorrhoids	33	...	....

TABLE 44. WHITE GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Hernia, femoral	10	...	....
Hernia, inguinal	16	...	....
Hernia, postoperative	19	3	15.8
Hernia, umbilical	21	...	....
Hernia, vaginal	1	...	....
Hernia, ventral	36	...	....
Hydatidiform mole	1	...	....
Hydro-appendix	1	...	....
Hydrocele, inguinal canal	1	...	....
Hydronephrosis	14	1	7.1
Hydrosalpinx	20	...	....
Hyperemesis gravidarum	2	...	....
Hyperesthesia	1	...	....
Hyperesthesia, vagina	1	...	....
Hyperesthesia, vulva	1	...	....
Hypernephroma	2	1	50.0
Hypertrophy, cervix	62	...	....
Hypertrophy and erosion of cervix	1	...	....
Hypertrophy, labia and clitoris	1	...	....
Hypertrophy and prolapse of uterus	1	...	....
Hysteria	5	...	....
Ileus	1	...	....
Imperforate hymen	1	...	....
Incontinence, urine	10	...	....
Infantile pelvic organs	3	...	....
Infantile uterus	2	...	....
Infection, puerperal	4	1	25.0
Infection, renal, bilateral	1	...	....
Infection, Skene's glands	3	...	....
Intestinal obstruction	6	2	33.3
Intestinal perforation	1	1	100.0
Jaundice	3	...	....
Kidney atrophy	1	...	....
Kraurosis vulvæ	1	...	....
Laceration, cervix	54	...	....
Leucorrhœa	34	...	....
Leukæmia, spleno-myelogenous	2	...	....
Malformation, pelvis	1	...	....
Menopause	1	...	....
Menorrhagia	45	...	....
Metrorrhagia	164	1	0.6
Morphinism	3	...	....
Movable spleen	1	...	....
Myoma, uterus	398	12	3.0
Necrosis, sacrum	1	...	....
Nephralgia	13	...	....
Nephritis	6	...	....
Nephrolithiasis	5	1	20.0
Nephroptosis	181	1	0.6
Neurasthenia	27	...	....
Neuritis	1	...	....
Osteomyelitis	1	...	....
Papilloma, bladder	5	...	....
Papilloma, ovary	3	...	....
Pelvic inflammatory disease	17	...	....

TABLE 44. WHITE GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Perihepatitis	1	...	....
Perimetritis	1	...	....
Periproctitis	1	...	....
Peritonitis, general	32	5	15.6
Peritonitis, pelvic	3	...	....
Periureteritis	1	...	....
Phlebitis	1	...	....
Polyp cervical	26	...	....
Polyp, rectal	1	...	....
Polyp, uterine	1	...	....
Polyp, vaginal	2	...	....
Polypoid endometrium	7	1	14.3
Pregnancy	100	1	1.0
Pregnancy, extra-uterine	114	3	2.6
Proctitis	7	...	....
Prolapse, ovary	12	...	....
Prolapse, rectum	2	...	....
Prolapse, uterus	130	1	0.8
Prolapse, vagina	6	...	....
Prolonged and irregular menstruation	1	...	....
Pruritus	2	...	....
Puerperal infection	6	1	16.7
Pyelitis	39	1	2.6
Pyelonephrosis	2	...	....
Pyometra	6	1	16.7
Pyonephrosis	13	2	15.4
Pyosalpinx	50	2	4.0
Pyuria	6	...	....
Rectocele	3	...	....
Redundant vaginal mucosa	1	...	....
Relaxed abdominal wall	2	...	....
Relaxed anal sphincter	1	...	....
Relaxed recti muscles	2	...	....
Relaxed urethral sphincter	2	...	....
Relaxed vaginal outlet	486	2	0.4
Retained secundines	176	...	....
Rheumatism	1	...	....
Rupture, recto-vaginal septum	14	1	7.1
Salpingitis	3	...	....
Salpingo-oophoritis	788	12	1.5
Sarcoma, ovary	3	...	....
Sarcoma, pelvis	1	...	....
Sarcoma, rectum	2	...	....
Sarcoma, uterus	2	...	....
Scar, ulcerated	1	...	....
Septicemia	2	1	50.0
Septicemia, puerperal	2	1	50.0
Sinus, abdominal	6	...	....
Sinus, abdomino-vaginal	1	...	....
Sinus, postoperative	16	...	....
Sinus from silver suture	1	...	....
Stenosis, internal os uteri	4	...	....
Stenosis, vaginal	1	...	....
Sterility	68	...	....
Stricture, rectum	5	...	....

TABLE 44. WHITE GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Stricture, ureter	3	...	....
Stricture, ureteral	11	...	....
Stricture, vagina	1	...	....
Syphilis	3	...	....
Syphilis, tertiary	1	...	....
Syphilitic periproctitis	1	...	....
Tear, sphincter ani	1	...	....
Tenesmus, rectal	1	...	....
Teratoma	1	...	....
Tonsillitis	1	...	....
Trigonitis	3	...	....
Tuberculosis, appendix	2	...	....
Tuberculosis, bladder	7	...	....
Tuberculosis, cervix	1	...	....
Tuberculosis, endometrium	2	...	....
Tuberculosis, kidney	31	2	6.5
Tuberculosis, kidney and ureter	2	...	....
Tuberculosis, miliary general	1	1	100.0
Tuberculosis, pelvic general	4	1	25.0
Tuberculosis, peritoneum	6	...	....
Tuberculosis, pulmonary	3	1	33.3
Tuberculosis, rectum	1	...	....
Tuberculosis, tubes and endometrium	2	...	....
Tuberculosis, tubes and ovaries	3	1	33.3
Tuberculosis, tubes and peritoneum	1	...	....
Tuberculosis, ureter	1	...	....
Tuberculous peritonitis	2	...	....
Tuberculous salpingitis	3	...	....
Tumor, abdominal	1	...	....
Tumor, liver	1	...	....
Tumor, ovarian	1	...	....
Tumor, pelvic	3	...	....
Ulcer, bladder	1	...	....
Ulcer, vagina	1	...	....
Ulceration, rectum and vagina, syphilitic	1	...	....
Urethritis	26	...	....
Uterus, anteflexion	10	...	....
Uterus, bicornate	1	...	....
Uterus, malformation	1	...	....
Uterus, punctured	1	...	....
Uterine retroposition	476	2	0.4
Uterine subinvolution	5	...	....
Vaginitis	21	...	....
Varicocele	1	...	....
Visceroptosis	1	...	....
Vulvitis	1	...	....
Wart, vaginal	1	...	....
*Unclassified	320	1	0.3

* Includes cases of doubtful terminology.

TABLE 45. SUMMARY OF WHITE OBSTETRICAL CASES FOR THE PERIOD 1904-1911.

Causes.	Admitted.	Died.	Per cent.
Labor, spontaneous at term	1265	3	0.2
Labor, spontaneous, premature	57	1	1.8
Labor, operative	332	15	4.5
Abortion	234	11	4.7
Admitted post-partum	48	8	16.7
Pregnant, not delivered	190	3	1.6
Not pregnant	35	0	0.0
Total	2161	41	1.9

	Admitted.		Died.	
	Number.	Per cent.	Number.	Per cent.
Labor, spontaneous at term	1265	58.5	3	7.3
Labor, spontaneous, premature	57	2.7	1	2.5
Labor, operative	332	15.4	15	36.6
Abortion	234	10.8	11	26.8
Admitted post-partum	48	2.2	8	19.5
Pregnant, not delivered	190	8.8	3	7.3
Not pregnant	35	1.6	0	0.0
Total	2161	100.0	41	100.0

SEC. F. MORTALITY RATE BY CAUSES ON ADMISSION, COLORED PATIENTS, 1902-1911.

TABLE 46. SUMMARY OF COLORED CASES.

	Males.			Females.		
Diseases and conditions.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	11	1	9.1	14	1	7.1
Blood	10	2	20.0	13	2	15.4
Bones and cartilages	78	2	2.6	40	2	5.0
Bursæ	3	...	....	3	...	....
Circulatory system	581	111	19.1	165	36	21.8
Arteries and veins	316	60	19.0	58	16	27.6
Endocardium and valves	214	44	20.6	89	17	19.1
Myocardium	45	6	13.3	17	3	17.6
Neuroses	...	...	....	...	...	....
Pericardium	6	1	16.7	1	...	....
Digestive system	387	31	8.0	441	41	9.3
Appendix	85	10	11.8	95	10	10.5
Intestine	43	7	16.3	38	8	21.1
Liver	39	4	10.3	9	1	11.1
Gall bladder and ducts	9	...	....	14	1	7.1
Mesentery	1	1	100.0	1	...	....
Omentum	...	...	....	1	...	....
Peritoneum	22	5	22.7	81	12	14.8
Lips	...	...	....	...	...	....
Mouth	3	1	33.3	2	...	....
Palate, uvula	...	...	....	...	...	....
Pharynx	2	1	50.0	1	...	....

TABLE 46. SUMMARY OF COLORED CASES—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Salivary glands	8	1	12.5	6	...	....
Teeth, gums	5	...	....	2	1	50.0
Tongue	...	...	....	2	...	....
Tonsils	26	...	....	46	1	2.2
Œsophagus	5	...	....	8	1	12.5
Pancreas	...	...	....	...	...	....
Rectum and anus	116	1	0.9	124	4	3.2
Stomach	23	...	....	11	2	18.2
Ductless glands and spleen	3	...	....	19	1	5.3
Carotid gland	...	...	....	...	...	....
Parathyroid gland	...	...	....	...	...	....
Pineal gland	...	...	....	...	...	....
Pituitary body	...	...	....	...	...	....
Spleen	...	...	....	...	...	....
Suprarenal gland	1	...	....	...	...	....
Thymus gland	...	...	....	...	...	....
Thyroid gland	2	...	....	19	1	5.3
Ear	11	...	....	10	...	....
Eye and adnexa	25	...	....	29	...	....
Infective diseases	997	144	14.4	598	61	10.2
Dysentery	10	1	10.0	2	1	50.0
Gonorrhœa	45	...	....	22	...	....
Influenza	12	...	....	9	...	....
Malaria	43	...	....	11	...	....
Rheumatic fever	29	...	....	29	1	3.4
Septicæmia	8	4	50.0	2	...	....
Syphilis	101	10	9.9	69	5	7.2
Tuberculosis, meninges	6	6	100.0	7	5	71.4
Tuberculosis, lungs	99	30	30.3	75	19	25.3
Tuberculosis, miliary	15	13	86.7	5	5	100.0
Tuberculosis, other forms	319	37	11.6	197	12	6.1
Typhoid fever	231	29	12.6	129	12	9.3
Other infective diseases	79	14	17.7	41	1	2.4
Herniæ	131	6	4.6	56	1	1.8
Joints	70	1	1.4	61	3	4.9
Lymphatic system	32	3	9.4	30	...	....
Mind	13	2	15.4	11	...	....
Miscellaneous	65	17	26.2	186	6	3.2
Diabetes	7	2	28.6	11	2	18.2
Gout	5	1	20.0	...	...	....
Obesity	1	...	....	3	...	....
Rheumatism, chronic articular	...	...	....	...	...	....
Rheumatism, n. s.	...	...	....	...	...	....
Other miscellaneous	52	14	26.9	172	4	2.3
Muscles, fasciæ, tendons	12	...	....	6	...	....
Muscles and fasciæ	8	...	....	2	...	....
Tendons and sheaths	4	...	....	4	...	....
Nervous system	112	21	18.7	94	28	29.8
Brain, spinal cord, meninges	63	21	33.3	43	24	55.8
Cranial and spinal nerves	10	...	....	9	...	....
Functional nervous disorders	39	...	....	42	4	9.5
Parasites	7	1	14.3	3	1	33.3
Poisonings and intoxications	8	1	12.5	6	1	16.7

TABLE 46. SUMMARY OF COLORED CASES—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Reproductive organs	81	12	14.8	1284	17	1.3
Functional disorders	...	...	....	99	...	....
Mammary gland	...	...	....	20	...	....
Ligaments, ovaries, tubes	...	...	....	953	15	1.6
Uterus	...	...	....	123	...	....
Vagina	...	...	....	73	2	2.7
Vulva	...	...	....	16	...	....
Cowper's glands	...	...	....	...	...	....
Penis	3	...	....	...	...	....
Prostate gland	36	11	30.6	...	...	....
Scrotum	7	1	14.3	...	...	....
Seminal vesicles	...	...	....	...	...	....
Spermatic cord	1	...	....	...	...	....
Testicle and epididymis	18	...	....	...	...	....
Tunica vaginalis	16	...	....	...	...	....
Respiratory system	391	70	17.9	137	29	21.2
Bronchi and trachea	33	1	3.0	26	...	....
Larynx and epiglottis	...	...	....	...	...	....
Lung	274	61	22.3	78	26	33.3
Nose and nasal passages	2	...	....	...	...	....
Accessory sinuses	...	...	....	...	...	....
Pleura	82	8	9.8	33	3	9.1
Skin, hair, nails	51	1	2.0	45	3	6.7
Skin and hair	51	1	2.0	43	3	7.0
Nails	...	...	....	2	...	....
Tumors	170	34	20.0	748	45	6.0
Benign	51	3	5.9	545	22	4.0
Malignant	119	31	26.1	203	23	11.3
Urinary organs	200	35	17.5	140	19	13.6
Bladder	15	3	20.0	39	...	....
Kidney	113	30	26.5	88	18	20.5
Ureter	1	...	....	...	...	....
Urethra	71	2	2.8	13	1	7.7
Obstetrical conditions	...	...	....	1868	30	1.6
Newborn child	1	...	....	...	...	....
Injuries	312	14	4.5	107	15	14.0
Grand total	3762	509	13.5	6114	342	5.6

TABLE 47. COLORED MEDICAL CASES.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	...	...	....	...	...	....
Blood	9	2	22.2	13	2	15.4
Bones and cartilages	3	...	....	1	...	....
Bursæ	1	...	....	...	...	....
Circulatory system	549	104	18.9	153	36	23.5
Arteries and veins	286	53	18.5	46	16	34.8
Endocardium and valves	213	44	20.7	89	17	19.1
Myocardium	45	6	13.3	17	3	17.6
Neuroses	...	...	....	...	...	....
Pericardium	5	1	20.0	1	...	....

TABLE 47. COLORED MEDICAL CASES—Continued

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Digestive system	102	6	5.9	62	5	8.1
Appendix	5	1	20.0	5	...	....
Intestine	14	...	....	12	1	8.3
Liver	33	2	6.1	6	1	16.7
Gall bladder and ducts	3	...	....	5	...	....
Mesentery	...	...	....	...	...	....
Omentum	...	...	....	...	...	....
Peritoneum	6	1	16.7	9	1	11.1
Lips	...	...	....	...	...	....
Mouth	2	1	50.0	1	...	....
Palate, uvula	...	...	....	...	...	....
Pharynx	...	...	....	1	...	....
Salivary glands	7	1	14.3	4	...	....
Teeth, gums	...	...	....	1	...	....
Tongue	...	...	....	...	...	....
Tonsils	16	...	....	10	1	10.0
Œsophagus	...	...	....	...	...	....
Pancreas	...	...	....	...	...	....
Rectum and anus	...	...	....	1	...	....
Stomach	16	...	....	7	1	14.3
Ductless glands and spleen	2	...	....	5	...	....
Carotid gland	...	...	....	...	...	....
Parathyroid gland	...	...	....	...	...	....
Pineal gland	...	...	....	...	...	....
Pituitary body	...	...	....	...	...	....
Spleen	...	...	....	...	...	....
Suprarenal gland	1	...	....	...	...	....
Thymus gland	...	...	....	...	...	....
Thyroid gland	1	...	....	5	...	....
Ear	2	...	....	1	...	....
Eye and adnexa	3	...	....	4	...	....
Infective diseases	606	95	15.7	360	50	13.9
Dysentery	9	1	11.1	2	1	50.0
Gonorrhœa	22	...	....	11	...	....
Influenza	12	...	....	9	...	....
Malaria	43	...	....	10	...	....
Rheumatic fever	29	...	...	29	1	3.4
Septicæmia	4	3	75.0	2	...	....
Syphilis	70	9	12.9	41	3	7.3
Tuberculosis, meninges	5	5	100.0	7	5	71.4
Tuberculosis, lungs	95	28	29.5	69	19	27.5
Tuberculosis, miliary	15	13	86.7	5	5	100.0
Tuberculosis, other forms	50	16	32.0	29	6	20.7
Typhoid fever	215	19	8.8	121	10	8.3
Other infective diseases	37	1	2.7	25	...	....
Herniæ	...	...	....	...	...	....
Joints	25	...	....	19	...	....
Lymphatic system	10	1	10.0	4	...	....
Mind	12	1	8.3	10	...	....
Miscellaneous diseases	35	13	37.1	34	4	11.8
Diabetes	7	2	28.6	10	2	20.0
Gout	5	1	20.0	...	...	....
Obesity	1	...	....	2	...	....

TABLE 47. COLORED MEDICAL CASES—Continued

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Rheumatism, chronic articular	...	...	....	...	...	....
Rheumatism, n. s.	...	...	....	...	...	....
Other miscellaneous	22	10	45.5	22	2	9.1
Muscles, fasciæ, tendons	7	...	....	1	...	....
Muscles and fasciæ	6	...	....	...	...	....
Tendons and sheaths	1	...	....	1	...	....
Nervous system	71	15	21.1	65	18	27.7
Brain, spinal cord, meninges	44	15	34.1	28	14	50.0
Cranial and spinal nerves	5	...	....	3	...	....
Functional nervous disorders	22	...	....	34	4	11.8
Parasites	3	...	....	...	...	....
Poisonings and intoxications	7	1	14.3	6	1	16.7
Reproductive organs	4	...	....	12	...	....
Functional disorders	...	...	....	...	...	....
Mammary gland	...	...	....	...	...	....
Ligaments, ovaries, tubes	...	...	....	10	...	....
Uterus	...	...	....	...	...	....
Vagina	...	...	....	2	...	....
Vulva	...	...	....	...	...	....
Cowper's glands	...	...	....	...	...	....
Penis	...	...	....	...	...	....
Prostate gland	2	...	....	...	...	....
Scrotum	...	...	....	...	...	....
Seminal vesicles	...	...	....	...	...	....
Spermatic cord	...	...	....	...	...	....
Testicle and epididymis	2	...	....	...	...	....
Tunica vaginalis	...	...	....	...	...	....
Respiratory system	368	66	17.9	125	26	20.8
Bronchi and trachea	33	1	3.0	26	...	....
Larynx and epiglottis	...	...	....	...	...	....
Lung	273	60	22.0	76	25	32.9
Nose and nasal passages	...	...	....	...	...	....
Accessory sinuses	...	...	....	...	...	....
Pleura	62	5	8.1	23	1	4.3
Skin, hair, nails	3	...	....	4	1	25.0
Skin and hair	3	...	....	4	1	25.0
Nails	...	...	....	...	...	....
Tumors	48	9	18.8	29	5	17.2
Benign	11	1	9.1	16	2	12.5
Malignant	37	8	21.6	13	3	23.1
Urinary organs	115	28	24.3	70	18	25.7
Bladder	1	...	....	1	...	....
Kidney	103	28	27.2	67	18	26.9
Ureter	...	...	....	...	...	....
Urethra	11	...	....	2	...	....
Obstetrical conditions	...	...	....	7	...	....
Newborn child	1	...	....	...	...	....
Injuries	2	1	50.0	1	...	....
Grand total	1988	342	17.2	986	166	16.8

TABLE 48. COLORED SURGICAL CASES.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent
Abnormities, congenital malformations	11	1	9.1	12	1	8.3
Blood	1	...	....	...	...	....
Bones and cartilages	75	2	2.7	39	2	5.1
Bursæ	2	...	....	3	...	....
Circulatory system	32	7	21.9	12	...	....
Arteries and veins	30	7	23.3	12	...	....
Endocardium and valves	1	...	....	...	...	....
Myocardium	...	...	....	...	...	....
Neuroses	...	...	....	...	...	....
Pericardium	1	...	....	...	...	....
Digestive system	285	25	8.8	207	19	9.2
Appendix	80	9	11.3	50	7	14.0
Intestine	29	7	24.1	19	4	21.1
Liver	6	2	33.3	3	...	....
Gall bladder and ducts	6	...	....	7	...	....
Mesentery	1	1	100.0	1	...	....
Omentum	...	...	....	...	...	....
Peritoneum	16	4	25.0	15	5	33.3
Lips	...	...	....	...	...	....
Mouth	1	...	....	1	...	....
Palate, uvula	...	...	....	...	...	....
Pharynx	2	1	50.0	...	...	....
Salivary glands	1	...	....	2	...	....
Teeth, gums	5	...	....	1	1	100.0
Tongue	...	...	....	2	...	....
Tonsils	10	...	....	36	...	....
Œsophagus	5	...	....	8	1	12.5
Pancreas	...	...	....	...	...	....
Rectum and anus	116	1	0.9	59	1	1.7
Stomach	7	...	....	3	...	....
Ductless glands and spleen	1	...	....	14	1	7.1
Carotid gland	...	...	....	...	...	....
Parathyroid gland	...	...	....	...	...	....
Pineal gland	...	...	....	...	...	....
Pituitary body	...	...	....	...	...	....
Spleen	...	...	....	...	...	....
Suprarenal gland	...	...	....	...	...	....
Thymus gland	...	...	....	...	...	....
Thyroid gland	1	...	....	14	1	7.1
Ear	9	...	....	9	...	....
Eye and adnexa	22	...	....	25	...	....
Infective diseases	391	49	12.5	197	10	5.1
Dysentery	1	...	....	...	...	....
Gonorrhœa	23	...	....	10	...	....
Influenza	...	...	....	...	...	....
Malaria	...	...	....	1	...	....
Rheumatic fever	...	...	....	...	...	....
Septicæmia	4	1	25.0	...	...	....
Syphilis	31	1	3.2	21	2	9.5
Tuberculosis, meninges	1	1	100.0	...	...	....
Tuberculosis, lungs	4	2	50.0	3	...	....
Tuberculosis, miliary	...	...	....	...	...	....

TABLE 48. COLORED SURGICAL CASES.—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Tuberculosis, other forms	269	21	7.8	148	6	4.1
Typhoid fever	16	10	62.5	2	1	50.0
Other infective diseases	42	13	31.0	12	1	8.3
Herniæ	131	6	4.6	33	1	3.0
Joints	45	1	2.2	42	3	7.1
Lymphatic system	22	2	9.1	16	...	....
Mind	1	1	100.0	1	...	....
Miscellaneous diseases	30	4	13.3	19	...	....
Diabetes	...	...	....	1	...	....
Gout	...	...	....	...	...	....
Obesity	...	...	....	1	...	....
Rheumatism, chronic articular	...	...	....	...	...	....
Rheumatism, n. s.	...	...	....	...	...	....
Other miscellaneous	30	4	13.3	17	...	....
Muscles, fasciæ, tendons	5	...	....	5	...	....
Muscles and fasciæ	2	...	....	2	...	....
Tendons and sheaths	3	...	....	3	...	....
Nervous system	41	6	14.6	26	10	38.5
Brain, spinal cord, meninges.	19	6	31.6	15	10	66.7
Cranial and spinal nerves	5	...	....	6	...	....
Funtional nervous disorders.	17	...	....	5	...	....
Parasites	4	1	25.0	2	...	....
Poisonings and intoxications	1	...	....	...	...	....
Reproductive organs	77	12	15.6	48	3	6.3
Functional disorders	...	...	....	...	...	....
Mammary gland	...	...	....	19	...	....
Ligaments, ovaries, tubes	...	...	....	26	3	11.5
Uterus	...	...	....	1	...	....
Vagina	...	...	....	2	...	....
Vulva	...	...	....	...	...	....
Cowper's glands	...	...	....	...	...	....
Penis	3	...	....	...	...	....
Prostate gland	34	11	32.4	...	...	....
Scrotum	7	1	14.3	...	...	....
Seminal vesicles	...	...	....	...	...	....
Spermatic cord	1	...	....	...	...	....
Testicle and epididymis	16	...	....	...	...	....
Tunica vaginalis	16	...	....	...	...	....
Respiratory system	23	4	17.4	11	3	27.3
Bronchi and trachea	...	...	....	...	...	....
Larynx and epiglottis	...	...	....	...	...	....
Lung	1	1	100.0	1	1	100.0
Nose and nasal passages	2	...	....	...	...	....
Accessory sinuses	...	...	....	...	...	....
Pleura	20	3	15.0	10	2	20.0
Skin, hair, nails	48	1	2.1	39	2	5.1
Skin and hair	48	1	2.1	37	2	5.4
Nails	...	...	....	2	...	....
Tumors	122	25	20.5	135	9	6.7
Benign	40	2	5.0	47	1	2.1
Malignant	82	23	28.0	88	8	9.1

TABLE 48. COLORED SURGICAL CASES.—Continued.

Diseases and conditions.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Urinary organs	85	7	8.2	9	...	....
Bladder	14	3	21.4	4	...	....
Kidney	10	2	20.0	5	...	....
Ureter	1	...	....	...	...	....
Urethra	60	2	3.3	...	...	....
Obstetrical conditions	...	...	....	3	...	....
Newborn child	...	...	....	...	...	....
Injuries	310	13	4.2	106	15	14.2
Grand total	1774	167	9.4	1013	79	7.8

TABLE 49. COLORED GYNECOLOGICAL CASES.

Diseases and conditions.	Admitted.	Died.	Per cent.
Abnormities, congenital malformations	2	...	....
Blood	....	...	....
Bones and cartilages	....	...	....
Bursæ	....	...	....
Circulatory system	....	...	....
Arteries and veins	....	...	....
Endocardium and valves	....	...	....
Myocardium	....	...	....
Neuroses	....	...	....
Pericardium	....	...	....
Digestive system	172	17	9.9
Appendix	40	3	7.5
Intestine	7	3	42.9
Liver	....	...	....
Gall bladder and ducts	2	1	50.0
Mesentery	....	...	....
Omentum	1	...	....
Peritoneum	57	6	10.5
Lips	....	...	....
Mouth	....	...	....
Palate, uvula	....	...	....
Pharynx	....	...	....
Salivary glands	....	...	....
Teeth, gums	....	...	....
Tongue	....	...	....
Tonsils	....	...	....
Œsophagus	....	...	....
Pancreas	....	...	....
Rectum and anus	64	3	4.7
Stomach	1	1	100.0
Ductless glands and spleen	....	...	....
Carotid gland	....	...	....
Parathyroid gland	....	...	....
Pineal gland	....	...	....
Pituitary body	....	...	....
Spleen	....	...	....
Suprarenal gland	....	...	....
Thymus gland	....	...	....
Thyroid gland	....	...	....
Ear	....	...	....

TABLE 49. COLORED GYNECOLOGICAL CASES—Continued.

Diseases and conditions.	Admitted.	Died.	Per cent.
Eye and adnexa	....	...	....
Infective diseases	41	1	2.4
Dysentery	....	...	....
Gonorrhœa	1	...	....
Influenza	....	...	....
Malaria	....	...	....
Rheumatic fever	....	...	....
Septicæmia	....	...	....
Syphilis	7	...	....
Tuberculosis, meninges	....	...	....
Tuberculosis, lungs	3	...	....
Tuberculosis, miliary	....	...	....
Tuberculosis, other forms	20	...	....
Typhoid fever	6	1	16.7
Other infective diseases	4	...	....
Herniæ	23	...	....
Joints	....	...	....
Lymphatic system	10	...	....
Mind	....	...	....
Miscellaneous diseases	133	2	1.5
Diabetes	....	...	....
Gout	....	...	....
Obesity	....	...	....
Rheumatism, chronic articular	....	...	....
Rheumatism, n. s.	....	...	....
Other miscellaneous	133	2	1.5
Muscles, fasciæ, tendons	....	...	....
Muscles and fasciæ	....	...	....
Tendons and sheaths	....	...	....
Nervous system	3	...	....
Brain, spinal cord, meninges	....	...	....
Cranial and spinal nerves	....	...	....
Functional nervous disorders	3	...	....
Parasites	1	1	100.0
Poisonings and intoxications	....	...	....
Reproductive organs	1224	14	1.1
Functional disorders	99	...	....
Mammary gland	1	...	....
Ligaments, ovaries, tubes	917	12	1.3
Uterus	122	...	....
Vagina	69	2	2.9
Vulva	16	...	....
Cowper's glands	....	...	....
Penis	....	...	....
Prostate gland	....	...	....
Scrotum	....	...	....
Seminal vesicles	....	...	....
Spermatic cord	....	...	....
Testicle and epididymis	....	...	....
Tunica vaginalis	....	...	....
Respiratory system	1	...	....
Bronchi and trachea	....	...	....
Larynx and epiglottis	....	...	....
Lung	1	...	....
Nose and nasal passages	....	...	....
Accessory sinuses	....	...	....
Pleura	....	...	....

TABLE 49. COLORED GYNECOLOGICAL CASES—Continued.

Diseases and conditions.	Admitted.	Died.	Per cent.
Skin, hair, nails	2	...	....
Skin and hair	2	...	....
Nails	....	...	....
Tumors	584	31	5.3
Benign	482	19	3.9
Malignant	102	12	11.8
Urinary organs	61	1	1.6
Bladder	34	...	....
Kidney	16	...	....
Ureter	....	...	....
Urethra	11	1	9.1
Obstetrical conditions	131	2	1.5
Newborn child	....	...	....
Injuries	....	...	....
Grand total	2388	69	2.9

TABLE 50. COLORED MEDICAL CASES.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abdominal pain	2	...	....	4	...	....
Abscess	2	...	....	...	...	....
Abscess, alveolar	...	...	....	1	...	....
Abscess, axillary	1	...	....	...	...	....
Abscess, cerebral	1	...	....	...	...	....
Abscess, liver	4	...	....	...	...	....
Abscess, liver, amœbic	1	...	....	...	...	....
Abscess, lung	...	...	....	2	1	50.0
Abscess, pelvic	...	...	....	2	...	....
Abscess, perirectal	...	...	....	1	...	....
Abscess, peritonsillar	...	...	....	1	...	....
Abscess, tonsillar	...	...	....	1	1	100.0
Addison's disease	1	...	....	...	...	....
Adenitis	2	...	....	1	...	....
Adenitis, cervical	2	...	....	...	...	....
Adenitis, inguinal	...	...	....	1	...	....
Adenitis, suppurative	3	...	....	...	...	....
Alcoholism	5	1	20.0	1	...	....
Anemia	3	...	....	...	...	....
Anemia, pernicious	4	1	25.0	2	...	....
Anemia, splenic	...	...	....	5	...	....
Aneurism, abdominal	1	1	100.0	...	...	....
Aneurism, abdominal aorta	1	...	....	...	...	....
Aneurism, aorta	47	8	17.0	5	2	40.0
Aneurism, innominate artery	1	1	100.0	...	...	....
Aneurism, thoracic	28	7	25.0	3	1	33.3
Appendicitis	5	1	20.0	5	...	....
Arteriosclerosis	205	36	17.6	37	12	32.4
Arthritis	5	...	....	2	...	....
Arthritis deformans	4	...	....	7	...	....
Arthritis, infectious	11	...	....	5	...	....
Arthritis, knee	1	...	....	1	...	....
Arthritis, villous	1	...	....	...	...	....
Asthma	9	...	....	6	...	....

TABLE 50. COLORED MEDICAL CASES—Continued.

Causes.	Males. Admitted.	Males. Died.	Males. Per cent.	Females. Admitted.	Females. Died.	Females. Per cent.
Asthma, bronchial	...	...	....	1	...	....
Atony, stomach	1	...	....	...	...	....
Atrophy, acute yellow	...	...	....	1	1	100.0
Atrophy, progressive muscular	1	...	....	...	...	....
Barlow's disease	...	...	....	1	...	....
Bronchiectasis	5	1	20.0	...	...	....
Bronchitis	19	...	....	19	...	....
Bursitis	1	...	....	...	...	....
Calculus, biliary	2	...	....	3	...	....
Calculus, renal	...	...	....	1	...	....
Carcinoma, bladder	2	...	....	...	...	....
Carcinoma, bile ducts	1	...	....	1	1	100.0
Carcinoma, breast	...	...	....	1	...	....
Carcinoma, liver	4	...	....	2	...	....
Carcinoma, lungs	1	1	100.0	...	...	....
Carcinoma, ovary	...	...	....	1	...	....
Carcinoma, pancreas	2	1	50.0	1	...	....
Carcinoma, prostate	2	...	....	...	...	....
Carcinoma, rectum	1	...	....	...	...	....
Carcinoma, seminal vesicle	1	...	....	...	...	....
Carcinoma, stomach	20	6	30.0	3	1	33.3
Carcinoma, uterus	...	...	....	2	1	50.0
Carcinomatosis	...	...	....	1	...	....
Cellulitis	1	...	....	...	...	....
Chancroid	2	...	....	1	...	....
Chicken-pox	...	...	....	3	...	....
Cholecystitis	1	...	....	1	...	....
Cholelithiasis	...	...	....	1	...	....
Chorea	2	...	....	4	...	....
Chorea, Huntingdon's	1	...	....	...	...	....
Cirrhosis, liver	15	2	13.3	4	...	....
Colitis	...	...	....	1	...	....
Colitis, ulcerative	...	...	....	1	...	....
Conjunctivitis	1	...	....	1	...	....
Constipation	2	...	....	3	...	....
Convulsions	...	...	....	1	1	100.0
Cryptorchidism	1	...	....	...	...	....
Cystitis	...	...	....	1	...	....
Cyst, ovarian	...	...	....	2	...	....
Degeneration of cord, posterior and pyramidal tracts	...	...	....	1	1	100.0
Delirium tremens	1	...	....	...	...	....
Dementia	1	...	....	5	...	....
Dermatitis	1	...	....	1	1	100.0
Dermatitis exfoliativa	1	...	....	...	...	....
Dermatomyositis	1	...	....	...	...	....
Diabetes mellitus	7	2	28.6	10	2	20.0
Diarrhœa	3	...	....	1	...	....
Dilatation, aorta	3	...	....	...	...	....
Dilatation, stomach	1	...	....	...	...	....
Diphtheria	9	1	11.1	2	...	....
Dysentery	3	...	....	1	...	....
Dysentery, amœbic	5	1	20.0	1	1	100.0
Dysentery, catarrhal	1	...	....	...	...	....

TABLE 50. COLORED MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Dyspepsia, nervous	1	...	....	...	...	....
Ectopia cordis interna	1	...	....	...	...	....
Embolus, cerebral	1	...	....	...	...	....
Empyema	4	...	....	...	...	....
Emphysema	5	...	....	...	...	....
Enlarged glands	1	...	....	...	...	....
Enteritis	3	...	....	1	1	100.0
Enteroptosis	...	...	....	1	...	....
Epididymitis	1	...	....	...	...	....
Epilepsy	4	...	....	1	...	....
Epilepsy, Jacksonian	1	...	....	...	...	....
Erysipelas	3	...	....	...	...	....
Febricula	12	...	....	12	...	....
Fever, continuous	6	...	....	4	...	....
Fever, malarial	43	...	....	10	...	....
Fever, paratyphoid	1	...	....	1	...	....
Fever, rheumatic	11	...	....	14	1	7.1
Fever, scarlet	1	...	....	1	...	....
Fever, typhoid	208	19	9.1	116	10	8.6
Fever, unknown origin	...	...	....	1	...	....
Fibroma, uterus	...	...	....	2	...	....
Fracture, vertebral	1	...	....	...	...	....
Fracture, wrist	...	...	....	1	...	....
Gangrene, toes	...	...	....	1	...	....
Gastralgia	...	...	....	1	...	....
Gastritis	9	...	....	2	...	....
Gastro-enteritis	5	...	....	2	...	....
Glaucoma	...	...	....	2	...	....
Glycosuria	1	...	....	...	...	....
Goitre, exophthalmic	1	...	....	3	...	....
Gonorrhœa	2	...	....	...	...	....
Gonorrhœal arthritis	20	...	....	11	...	....
Gout	5	1	20.0	...	...	....
Heart diseases.						
Aortic insufficiency	77	19	24.7	10	3	30.0
Aortic and cardiac insufficiency	1	...	....	...	...	....
Aortic and mitral insufficiency	74	8	10.8	22	4	18.2
Aortic, mitral and myocardial insufficiency	1	...	....	4	...	....
Aortic and myocardial insufficiency	3	1	33.3	3	2	66.7
Aortic and mitral insufficiency and stenosis	5	1	20.0	2	...	....
Aortic, mitral and tricuspid insufficiency, and mitral stenosis	...	...	....	1	1	100.0
Aortic stenosis	2	...	....	1	...	....
Aortic stenosis and insufficiency	1	...	....	1	1	100.0
Cardiac decompensation	...	...	....	1	...	....
Endocarditis	15	11	73.3	4	2	50.0
Mitral insufficiency	21	1	4.8	13	4	30.8
Mitral and myocardial insufficiency	1	...	....	1	...	....
Mitral and myocardial insufficiency and stenosis	...	...	....	1	...	....

TABLE 50. COLORED MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Mitral stenosis	1	...	....	3	...	....
Mitral stenosis and insufficiency	9	2	22.2	19	...	....
Mitral and tricuspid insufficiency	2	1	50.0	3	...	....
Myocardial insufficiency	6	...	....	...	...	....
Myocarditis	35	6	17.1	17	3	17.6
Pericarditis	5	1	20.0	1	...	....
Stokes-Adams syndrome	1	...	....	...	...	....
Hematuria	2	...	....	...	...	....
Hemichorea	...	...	....	1	1	100.0
Hemiplegia	8	...	....	9	4	44.4
Hemiplegia, infantile	...	...	....	1	...	....
Hemoglobinuria	...	...	....	1	...	....
Hemorrhage	2	2	100.0	1	...	....
Hemorrhage, cerebral	2	2	100.0	2	2	100.0
Hepatitis	...	...	....	1	...	....
Herpes zoster	1	...	....	...	...	....
Hodgkin's disease	2	1	50.0	...	...	....
Hyperacidity	...	...	....	1	1	100.0
Hypernephroma	...	...	....	1	...	....
Hyperthyroidism	...	...	....	1	...	....
Hypertrophy, prostate	1	...	....	...	...	....
Hysteria	1	...	....	11	...	....
Imbecility	1	...	....	...	...	....
Impetigo	...	...	....	3	...	....
Infarction, pulmonary	...	...	....	1	...	....
Infection, strongyloides intestinalis	1	...	....	...	...	....
Influenza	12	...	....	9	...	....
Insanity	1	...	....	...	...	....
Intestinal hemorrhage	1	...	....	...	...	....
Jaundice	2	...	....	...	...	....
Jaudice, catarrhal	12	...	....	...	...	....
Leukæmia	1	...	....	4	2	50.0
Leukæmia, lymphatic	1	1	100.0	...	...	....
Locomotor ataxia	2	1	50.0	...	...	....
Lues	1	...	....	...	...	....
Lues, cerebral	5	...	....	4	...	....
Lues, secondary	11	...	....	3	...	....
Lues, tertiary	10	2	20.0	2	...	....
Lympho-sarcoma	1	...	....	...	...	....
Malnutrition	...	...	....	1	1	100.0
Mania	1	...	....	1	...	....
Measles	4	...	....	1	...	....
Mediastinitis	1	...	....	...	...	....
Meningitis	15	9	60.0	7	4	57.1
Meningitis, cerebro-spinal	6	3	50.0	3	2	66.7
Mikulicz's disease	1	...	....	...	...	....
Myalgia	2	...	....	...	...	....
Myelitis	...	...	....	1	1	100.0
Myoma, uterus	...	...	....	4	2	50.0
Myomata	...	...	....	1	...	....
Myxœdema	...	...	....	1	...	....
Neoplasm	1	...	....	...	...	....
Nephritis	100	28	28.0	56	17	30.4

Table 50. Colored Medical Cases—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Neuralgia	1	...	....	...	...	....
Neurasthenia	10	...	....	13	...	....
Neuritis, optic	...	...	....	1	...	....
Neuritis, peripheral	1	...	....	1	...	....
Neuro-fibromata	...	...	....	2	...	....
Neurosis	1	...	....	1	...	....
Obesity	1	...	....	2	...	....
Osteoarthritis	1	...	....	...	...	....
Osteomyelitis	1	...	....	...	...	....
Otitis media	2	...	....	1	...	....
Palsy	...	...	....	1	...	....
Panophthalmitis	1	...	....	...	...	....
Paralysis	1	...	....	2	2	100.0
Paralysis, bulbar	...	...	....	1	...	....
Paralysis, obstetrical	...	...	....	1	...	....
Paramyoclonus multiplex	1	...	....	...	...	....
Paraplegia, spastic	3	...	....	...	...	....
Parotitis	3	...	....	3	...	....
Pellagra	2	1	50.0	1	...	....
Pelvic disease	...	...	....	1	...	....
Periostitis	1	...	....	1	...	....
Peritonitis	6	1	16.7	6	1	16.7
Peritonitis, pelvic	...	...	....	3	...	....
Pertussis	2	...	....	2	...	....
Pharyngitis	...	...	....	1	...	....
Phlebitis	2	...	....	...	...	....
Pleura, thickened	2	...	....	1	...	....
Pleurisy	1	...	....	...	...	....
Pleurisy, adhesive	1	...	....	...	...	....
Pleurisy, diaphragmatic	2	...	....	...	...	....
Pleurisy with effusion	42	4	9.5	13	1	7.7
Pleurisy, fibrinous	9	1	11.1	9	...	....
Pleurisy and peritonitis, tuberculous	1	...	....	2	...	....
Pleurisy, peritonitis and pericarditis, tuberculous	2	...	....	...	...	....
Pneumonia	21	2	9.5	4	1	25.0
Pneumonia, broncho-	8	4	50.0	11	7	63.6
Pneumonia, lobar	239	54	22.6	58	16	27.6
Poisoning, alcoholic	1	...	....	...	...	....
Poisoning, carbolic acid	1	...	....	2	...	....
Poisoning, coal-gas	1	...	....	...	...	....
Poisoning, creosote	...	...	....	2	...	....
Poisoning, lead	2	...	....	...	...	....
Poisoning, mercurial	...	...	....	1	1	100.0
Poliomyelitis	2	...	....	...	...	....
Polyarthritis	2	...	....	4	...	....
Polyneuritis	...	...	....	1	...	....
Polyserositis	4	1	25.0	2	...	....
Pott's disease	2	...	....	1	...	....
Pregnancy	...	...	....	5	...	....
Premature birth	1	...	....	...	...	....
Prolapse, colon	...	...	....	2	...	....
Prostatitis	1	...	....	...	...	....

Table 50. Colored Medical Cases—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Psychoneurosis	2	...	....	3	...	....
Purpura	...	...	....	2	...	....
Pyelitis	...	...	....	5	...	....
Pyelonephritis	...	...	....	1	...	....
Pyelonephrosis	...	...	....	1	...	....
Pyonephrosis	...	...	....	1	...	....
Pyuria	1	...	....	...	...	....
Quinsy	...	...	....	1	...	....
Rachitis	2	...	....	1	...	....
Recklinghausen's disease	...	...	....	2	...	....
Relaxation, sacro-iliac	1	...	....	...	...	....
Rheumatism	17	...	....	13	...	....
Rheumatism, acute articular	1	...	....	2	...	....
Rupture, bladder	1	1	100.0	...	...	....
Salpingo-oophoritis	...	...	....	8	...	....
Sarcomatosis	1	...	....	...	...	....
Sciatica	2	...	....	1	...	....
Separation, symphysis	1	...	....	...	...	....
Septicæmia	4	3	75.0	1	...	....
Septico-pyæmia	...	...	....	1	...	....
Small-pox	1	...	....	1	...	....
Stenosis, pyloric	1	...	....	...	...	....
Stomatitis	2	1	50.0	1	...	....
Stricture, rectum	...	...	....	1	...	....
Syphilis	42	7	16.7	32	3	9.4
Syphilis, cerebral	1	...	....	...	...	....
Syringomyelia	3	...	....	1	...	....
Tabes dorsalis	2	...	....	1	...	....
Tenosynovitis	...	...	....	1	...	....
Tetany	3	...	....	2	...	....
Thrombosis	...	...	....	1	1	100.0
Tonsillitis	16	...	....	7	...	....
Torticollis	2	...	....	...	...	....
Tuberculosis	1	...	....	1	...	....
Tuberculosis, ankle	...	...	....	1	...	....
Tuberculosis, brain, intestines and liver	...	...	....	1	1	100.0
Tuberculosis, elbow	1	...	....	...	...	....
Tuberculosis, Fallopian tube	...	...	....	1	1	100.0
Tuberculosis, general	11	9	81.8	2	1	50.0
Tuberculosis, intestines	1	1	100.0	...	...	....
Tuberculosis, lymph glands	3	1	33.3	1	...	....
Tuberculosis, miliary	15	13	86.7	5	5	100.0
Tuberculosis, peritoneal	1	...	....	1	1	100.0
Tuberculosis, pleural and peritoneal	2	...	....	1	1	100.0
Tuberculosis, pulmonary	80	25	31.3	62	15	24.2
Tuberculosis, pulmonary and intestinal	1	1	100.0	2	2	100.0
Tuberculosis, pulmonary and laryngeal	3	...	....	...	...	....
Tuberculosis, pulmonary and peritoneal	1	...	....	...	...	....
Tuberculosis, serous membrane	1	1	100.0	...	...	....
Tuberculosis, skull	...	...	....	1	...	....

TABLE 50. COLORED MEDICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Tuberculosis, spine	4	1	25.0	...	...	....
Tuberculosis, sternum	1	...	....	1	...	....
Tuberculous adenitis	6	1	16.7	...	...	....
Tuberculous arthritis	2	...	....	1	...	....
Tuberculous meningitis	5	5	100.0	6	4	66.7
Tuberculous pericarditis	3	1	33.3	7	1	14.3
Tuberculous peritonitis	13	1	7.7	12	2	16.7
Tuberculous pleurisy	1	...	....	...	...	....
Tuberculous pneumonia	3	2	66.7	1	1	100.0
Tuberculous spondylitis	1	...	....	...	...	....
Tumor, abdominal	2	...	....	1	...	....
Tumor, cerebral	5	1	20.0	1	...	....
Tumor, intra-thoracic	1	...	....	...	...	....
Tumor, mediastinal	1	...	....	3	...	....
Tumor, neck	1	...	....	...	...	....
Tumor, spinal cord	1	...	....	...	...	....
Ulcer, gastric	3	...	....	2	...	....
Ulcer, leg	1	...	....	...	...	....
Uncinariasis	2	...	....	...	...	....
Uremia	1	...	....	1	1	100.0
Urethritis	11	...	....	2	...	....
Vaginitis	...	...	....	2	...	....
Vomiting	...	...	....	1	...	....
Vomiting, pregnancy	...	...	....	1	...	....
*Unclassified	9	8	88.9	9	1	11.1

TABLE 51. COLORED SURGICAL CASES.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Abdominal pain	2	...	....	1	...	....
Abscess, abdominal wall	4	...	....	2	...	....
Abscess, alveolar	4	...	....	...	...	....
Abscess, ankle	2	...	....	...	...	....
Abscess, arm	2	...	....	2	...	....
Abscess, axillary	4	...	....	3	...	....
Abscess, back	...	...	....	4	...	....
Abscess, breast	...	...	....	8	...	....
Abscess, buttocks	2	...	....	1	...	....
Abscess, cerebral	1	1	100.0	1	...	....
Abscess, cervical	2	...	....	2	...	....
Abscess, cheek	2	...	....	1	...	....
Abscess, chest	2	...	....	...	...	....
Abscess, face	1	...	....	...	...	....
Abscess, groin	1	1	100.0	...	...	....
Abscess, hip	1	...	....	...	...	....
Abscess, intra-abdominal	1	...	....	2	...	....
Abscess, intra-orbital	...	...	....	1	...	....
Abscess, ischio-rectal	2	...	....	1	...	....
Abscess, jaw	1	...	....	1	...	....
Abscess, knee	1	...	....	...	...	....
Abscess, leg	7	...	....	4	...	....
Abscess, liver	5	2	40.0	1	...	....

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* Includes cases of doubtful terminology.

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent
Abscess, liver, amœbic	1	1	100.0	...	...	....
Abscess, lumbar	1	...	....	...	...	....
Abscess, mastoid	...	...	....	2	...	....
Abscess, neck	10	...	....	7	...	....
Abscess, palmar	1	...	....	...	...	....
Abscess, pelvic	...	...	....	1	1	100.0
Abscess, perineal	4	1	25.0	...	...	....
Abscess, perirectal	24	...	....	13	1	7.7
Abscess, peritonsillar	2	...	....	...	...	....
Abscess, periurethral	10	1	10.0	...	...	....
Abscess, popliteal	1	...	....	...	...	....
Abscess, postauricular	1	...	....	...	...	....
Abscess, prostate	1	1	100.0	...	...	....
Abscess, psoas	2	...	....	...	...	....
Abscess, retroperitoneal	1	...	....	...	...	....
Abscess, retropharyngeal	2	1	50.0	...	...	....
Abscess, scalp	1	...	....	1	1	100.0
Abscess, scrotum	1	...	....	...	...	....
Abscess, shoulder	1	...	....	...	...	....
Abscess, submental	1	...	....	...	...	....
Abscess, thigh	5	...	....	1	...	....
Abscess, tibia	1	...	....	...	...	....
Abscess, tongue	...	...	....	1	...	....
Abscess, tonsillar	...	...	....	1	...	....
Abscess, urachus	...	...	....	1	...	....
Abscess, multiple	2	...	....	1	...	....
Actinomycosis	3	1	33.3	1	...	....
Actinomycosis, jaw	1	...	....	...	...	....
Adenitis, axillary, infectious	...	...	....	1	...	....
Adenitis, axillary, suppurative	2	...	....	...	...	....
Adenitis, cervical	2	1	50.0	2	...	....
Adenitis, cervical, suppurative	...	...	....	1	...	....
Adenitis, inguinal	8	...	....	5	...	....
Adenitis, inguinal, chancroidal	3	...	....	...	...	....
Adenitis, inguinal, suppurative	7	...	....	2	...	....
Adeno-carcinoma, palate	1	...	....	...	...	....
Adeno-fibroma	...	...	....	1	...	....
Adenoids	1	...	....	...	...	....
Adenoma	...	...	....	1	...	....
Adhesions	...	...	....	1	...	....
Adiposis	...	...	....	1	...	....
Ainhum	1	...	....	...	...	....
Alcoholism, chronic	1	1	100.0	...	...	....
Amputation, leg, traumatic	1	...	....	...	...	....
Amputation, stump	1	...	....	...	...	....
Anæmia	1	...	....	...	...	....
Aneurism	19	5	26.3	...	...	....
Aneurism, popliteal	1	...	....	...	...	....
Angio-fibroma	...	...	....	1	...	....
Angioma	2	...	....	1	...	....
Ankylosis	...	...	....	1	...	....
Ankylosis, knee	1	...	....	...	...	....
Aortitis	1	1	100.0	...	...	....
Apoplexy	1	1	100.0	2	2	100.0

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Appendicitis	80	9	11.2	50	7	14.0
Arthritis deformans	...	...	....	1	...	....
Arthritis, elbow	1	...	....	...	...	....
Arthritis, hip	1	...	....	1	...	....
Arthritis, infectious	8	...	....	8	...	....
Arthritis, knee	2	...	....	...	...	....
Arthritis, knee, infectious	...	...	....	2	2	100.0
Arthritis, knee, purulent	1	...	....	...	...	....
Arthritis, knee, rheumatoid	...	...	....	1	...	....
Arthritis, knee, suppurative	1	1	100.0	...	...	....
Arthritis, knee, traumatic	1	...	....	...	...	....
Arthritis, knee, villous	2	...	....	...	...	....
Arthritis, metatarso-phalangeal joint	2	...	....	...	...	....
Arthritis, villous	1	...	....	2	...	....
Ascites	1	...	....	...	...	....
Buboes	...	...	....	1	...	....
Bullet in foot	1	...	....	...	...	....
Burns	4	...	....	8	3	37.5
Burn, superficial	16	...	....	19	8	42.1
Bursitis	2	...	....	3	...	....
Calculus, biliary	3	...	....	5	...	....
Calculus, ureteral	1	...	....	...	...	....
Calculus, vesical	6	2	33.3	...	...	....
Carcinoma, antrum	1	...	....	1	...	....
Carcinoma, back	...	...	....	1	...	....
Carcinoma, bladder	2	1	50.0	...	...	....
Carcinoma, breast	1	...	....	54	1	1.9
Carcinoma, cæcum	1	...	....	...	...	....
Carcinoma, cervical glands	2	1	50.0	1	...	....
Carcinoma, chest wall	...	...	....	1	...	....
Carcinoma, gall bladder	1	1	100.0	1	...	....
Carcinoma, inguinal glands	1	1	100.0	...	...	....
Carcinoma, intestines	3	...	....	2	1	50.0
Carcinoma, liver	1	...	....	...	...	....
Carcinoma, lung	2	2	100.0	...	...	....
Carcinoma, maxilla	1	...	....	...	...	....
Carcinoma, mouth	1	...	....	...	...	....
Carcinoma, nasopharynx	5	1	20.0	1	...	....
Carcinoma, neck	2	...	....	...	...	....
Carcinoma, pancreas	1	1	100.0	3	2	66.7
Carcinoma, penis	6	2	33.3	...	...	....
Carcinoma, prostate	4	1	25.0	...	...	....
Carcinoma, rectum	7	3	42.9	1	...	....
Carcinoma, scalp	...	...	....	1	...	....
Carcinoma, sigmoid	2	...	....	...	...	....
Carcinoma, stomach	13	7	53.8	2	...	....
Carcinoma, tongue	1	...	....	...	...	....
Carcinoma, tonsils	...	...	....	1	1	100.0
Carcinosis	...	...	....	1	1	100.0
Cellulitis	28	3	10.7	9	1	11.1
Chancroids	7	...	....	...	...	....
Cholecystitis	2	...	....	2	...	....
Cirrhosis, liver	1	...	....	2	...	....
Cleft palate	1	...	....	1	1	100.0

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Club-foot	3	...	....	3	...	....
Colitis	1	...	....	...	...	....
Concussion, brain	1	...	....	...	...	....
Condyloma	1	...	....	...	...	....
Constipation	...	...	....	1	...	....
Contracture, foot, following burn	1	...	....	...	...	....
Contracture, hand	...	...	....	2	...	....
Contractures	3	...	....	...	...	....
Contusions	12	...	....	3	...	....
Contusion, abdomen	3	...	....	1	...	....
Contusion, back	1	...	....	...	...	....
Contusion, elbow	1	...	....	...	...	....
Contusion, flank	1	...	....	1	...	....
Contusion, head	4	...	....	2	...	....
Contusion, hip	2	...	....	...	...	....
Contusion, knee	2	...	....	...	...	....
Contusion, shoulder	...	...	....	1	...	....
Contusion, thorax	2	...	....	...	...	....
Contusion, general	1	...	....	...	...	....
Convulsion, cerebral	1	...	....	...	...	....
Coxa vara	3	...	....	3	...	....
Cyst, breast	...	...	....	7	...	....
Cyst, dentigerous	1	...	....	1	1	100.0
Cyst, femur	...	...	....	1	1	100.0
Cyst, mesenteric	...	...	....	1	...	....
Cysts, neck	2	...	....	2	...	....
Cyst, thyroglossal duct	...	...	....	1	...	....
Cyst, thyroid gland	...	...	....	2	...	....
Cystitis	6	1	16.7	4	...	....
Deformity, ears	1	...	....	...	...	....
Deformity, face	1	...	....	...	...	....
Dermatitis, blastomycetic	5	...	....	1	...	....
Diabetes	...	...	....	1	...	....
Dilatation, colon	1	...	....	...	...	....
Diphtheria	2	...	....	...	...	....
Dislocation, elbow	1	...	....	...	...	....
Dislocation, femur	1	...	....	...	...	....
Dislocation, hip	6	...	....	1	...	....
Dislocation, humerus	1	...	....	...	...	....
Dislocation, semilunar cartilage	1	...	....	...	...	....
Dislocation, shoulder	5	...	....	3	...	....
Dislocations	4	...	....	...	...	....
Dysentery, amœbic	1	...	....	...	...	....
Eczema	...	...	....	1	...	....
Embolism, cerebral	1	...	....	...	...	....
Empyema	15	2	13.3	10	2	20.0
Encephalocystocele	...	...	....	1	1	100.0
Endocarditis	1	...	....	...	...	....
Enteritis	2	...	....	1	...	....
Epididymitis	16	...	....	...	...	....
Epilepsy	6	...	....	1	...	....
Epiphysitis	1	...	....	1	...	....
Episcleritis	...	...	....	1	...	....
Epistaxis	1	...	....	...	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Ad-mitted.	Died.	Per cent.	Ad-mitted.	Died.	Per cent.
Epithelioma	5	...	....	2	...	....
Epithelioma, arm	...	...	....	1	1	100.0
Epithelioma, lip	...	...	....	1	...	....
Erysipelas	...	...	....	3	...	....
Erythema	...	...	....	1	...	....
Exostosis	...	...	....	1	...	....
Exostosis, femur	2	...	....	1	...	....
Exostosis, os calcis	1	...	....	...	...	....
Fever, malaria	...	...	....	1	...	....
Fever, typhoid	15	9	60.0	2	1	50.0
Fever, typhoid (intestinal perforation)	1	1	100.0	...	...	....
Fibro-adenoma, breast	...	...	....	1	...	....
Fibro-carcoma	...	...	....	1	...	....
Fibroma, rectus muscle	...	...	....	1	...	....
Fibromata, multiple	1	...	....	...	...	....
Fissure in ano	2	...	....	8	...	....
Fistula in ano	45	...	....	14	...	....
Fistula, fecal	1	...	....	2	1	50.0
Fistula, perineal	2	...	....	...	...	....
Fistula, urethral	5	...	....	...	...	....
Flat-foot	2	...	....	4	...	....
Floating cartilage in knee	1	...	....	...	...	....
Foreign body in brain	1	...	....	...	...	....
Foreign body in foot	...	...	....	1	...	....
Foreign body in gastro-intestinal tract	...	...	....	1	...	....
Foreign body in œsophagus	...	...	....	1	...	....
Fracture, arm	1	...	....	...	...	....
Fracture, clavicle	1	...	....	...	...	....
Fracture, Colles'	3	...	....	1	...	....
Fracture, femur	25	2	8.0	14	1	7.1
Fracture, fibula	3	...	....	2	...	....
Fracture, frontal bone	1	...	....	...	...	....
Fracture, humerus	7	...	....	4	...	....
Fracture, jaw	1	...	....	1	...	....
Fracture, malleolus	2	...	....	...	...	....
Fracture, maxilla	1	...	....	...	...	....
Fracture, metacarpal bone	1	...	....	...	...	....
Fracture, metatarsals	1	...	....	...	...	....
Fracture, nose	3	...	....	1	...	....
Fracture, olecranon	...	...	....	1	...	....
Fracture, patella	3	...	....	4	...	....
Fracture, pelvis	4	1	25.0	...	...	....
Fracture, phalanges	2	...	....	...	...	....
Fracture, Pott's	11	...	....	1	...	....
Fracture, radius	...	...	....	1	1	100.0
Fracture, radius and ulna	3	...	....	1	...	....
Fracture, ribs	6	1	16.7	1	...	....
Fracture, scapula	...	...	....	1	...	....
Fracture, skull	11	1	9.1	3	1	33.3
Fracture, tarsus	2	...	....	...	...	....
Fracture, tibia	15	...	....	1	...	....
Fracture, tibia and fibula	16	...	....	4	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Fracture, toe	1	...	....	...	...	....
Fracture, ulna	3	...	....	...	...	....
Fracture, vertebra	3	3	100.0	...	...	....
Fracture, wrist	1	...	....	...	...	....
Frost bite	6	...	....	...	...	....
Gangrene	9	...	....	1	...	....
Gastro-enteritis	1	...	....	1	...	....
Genu valgum	15	...	....	17	...	....
Genu varum	7	...	....	10	...	....
Giant colon	2	...	....	2	...	....
Glaucoma	1	...	....	...	...	....
Goitre	...	...	....	3	...	....
Goitre, colloid	...	...	....	3	...	....
Goitre, exophthalmic	1	...	....	6	1	16.7
Gonorrhœa	1	...	....	...	...	....
Gonorrhœal arthritis	8	...	....	5	...	....
Gonorrhœal arthritis, ankle	2	...	....	1	...	....
Gonorrhœal arthritis, elbow	1	...	....	...	...	....
Gonorrhœal arthritis, knee	6	...	....	3	...	....
Gonorrhœal arthritis, shoulder	2	...	....	...	...	....
Gonorrhœal arthritis, wrist	1	...	....	...	...	....
Gonorrhœal inguinal adenitis	1	...	....	...	...	....
Gonorrhœal ophthalmia	1	...	....	...	...	....
Gonorrhœal peritonitis	...	...	....	1	...	....
Gumma	3	...	....	1	1	100.0
Gumma, arm	...	...	....	1	...	....
Gumma, larynx	...	...	....	1	...	....
Gumma, liver	1	...	....	...	...	....
Gumma, nares	...	...	....	1	...	....
Gumma, ribs	1	...	....	...	...	....
Gumma, testicle	1	...	....	...	...	....
Gumma, tibia	1	...	....	...	...	....
Hammer toe	...	...	....	1	...	....
Harelip	5	1	20.0	1	...	....
Hemangioma	1	...	....	...	...	....
Hematoma	4	...	....	...	...	....
Hematomyelia	5	1	20.0	...	...	....
Hematuria	5	1	20.0	...	...	....
Hemorrhage	3	2	66.7	2	...	....
Hemorrhage, intracranial	1	...	....	2	2	100.0
Hemorrhages, postoperative	1	...	....	...	...	....
Hemorrhage, traumatic	1	...	....	...	...	....
Hemorrhoids	31	...	....	6	...	....
Hernia, femoral	1	...	....	8	1	12.5
Hernia, inguinal	83	1	1.2	12	...	....
Hernia, inguinal, double	3	...	....	...	...	....
Hernia, inguinal, left	4	...	....	2	...	....
Hernia, inguinal, right	11	...	....	1	...	....
Hernia, inguinal, strangulated	21	3	14.3	1	...	....
Hernia, umbilical	1	...	....	8	...	....
Hernia, umbilical, strangulated	1	1	100.0	1	...	....
Hernia, ventral	5	...	....	...	...	....
Hirschsprung's disease	...	...	....	1	...	....
Hodgkin's disease	1	1	100.0	2	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Hydrocele	16	...	....	2	...	....
Hydrocephalus	1	...	....	2	2	100.0
Hydronephrosis	1	1	100.0	...	...	....
Hypernephroma	...	...	....	1	...	....
Hypertrophy	1	1	100.0	...	...	....
Hypospadias	1	...	....	...	...	....
Hysteria	...	...	....	2	...	....
Infected arm	1	...	....	...	...	....
Infected keloid	1	...	....	...	...	....
Ingrowing toe-nail	...	...	....	2	...	....
Intestinal obstruction	13	5	38.5	8	2	25.0
Intestinal obstruction, volvulus	1	1	100.0	...	...	....
Insanity	...	...	....	1	...	....
Jaundice	1	1	100.0	...	...	....
Keloid	8	...	....	5	...	....
Keloid, breast	...	...	....	1	...	....
Keloid, face and scalp	1	...	....	...	...	....
Laceration, hand	2	...	....	...	...	....
Laceration, penis	1	...	....	...	...	....
Lacerations	4	...	....	1	...	....
Lipoma	2	...	....	6	...	....
Lipoma, back	...	...	....	1	...	....
Lipoma, groin	1	...	....	...	...	....
Lipoma, loin	...	...	....	2	...	....
Lipoma, shoulder	1	...	....	4	...	....
Lipoma, thigh	3	...	....	1	...	....
Loose cartilage in knee	1	...	....	...	...	....
Lues	1	...	....	...	...	....
Lumbago	3	...	....	...	...	....
Lupus vulgaris	...	...	....	1	...	....
Lymphangioma	2	...	....	1	...	....
Mammitis	...	...	....	1	...	....
Mastitis	1	...	....	3	...	....
Mastoiditis	5	...	....	4	...	....
Meningitis	2	2	100.0	2	2	100.0
Myelitis	1	...	....	...	...	....
Myoma, uteri	...	...	....	2	...	....
Myositis	2	...	....	1	...	....
Myxoma	1	...	....	6	...	....
Myxoma, breast	...	...	....	1	...	....
Myxoma, intracanalicular	...	...	....	2	...	....
Myxo-sarcoma	...	...	....	2	...	....
Necrosis, skull	...	...	....	1	...	....
Necrosis, superior maxilla	1	...	....	...	...	....
Nephritis	3	...	....	2	...	....
Neuralgia	...	...	....	1	...	....
Neuralgia, facial	3	...	....	5	...	....
Neuralgia, intercostal	1	...	....	...	...	....
Neurasthenia	4	...	....	2	...	....
Neurosis	2	...	....	...	...	....
Neurosis, posttraumatic	1	...	....	...	...	....
New growth of cervical glands	1	...	....	...	...	....
Obstruction, intestines	3	...	....	3	1	33.3
Œdema	...	...	...	1	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Osteitis	1	...	....	...	...	....
Osteoarthritis	4	...	....	...	...	....
Osteoma	1	...	....	2	...	....
Osteomyelitis	24	1	4.2	14	1	7.1
Osteomyelitis, femur	1	...	....	...	...	....
Osteomyelitis, fibula	...	...	....	1	...	....
Osteomyelitis, humerus	1	...	....	...	...	....
Osteomyelitis, inferior maxilla	2	...	....	1	...	....
Osteomyelitis, patella	1	...	....	...	...	....
Osteomyelitis, phalanx	1	...	....	1	...	....
Osteomyelitis, tibia	...	...	....	1	...	....
Otitis media	1	...	....	1	...	....
Oxycephaly	...	...	....	1	...	....
Painful ankle	...	...	....	1	...	....
Papilloma, rectum	...	...	....	1	...	....
Paralysis, facial	1	...	....	...	...	....
Paralysis, obstetrical	...	...	....	1	...	....
Paraphimosis	1	...	....	...	...	....
Paraplegia, spastic	1	...	....	...	...	....
Pelvic inflammatory disease	...	...	....	3	...	....
Pericarditis	1	...	....	...	...	....
Pericholecystitis	1	...	....	...	...	....
Periostitis	6	...	....	...	...	....
Periostitis, femur	1	...	....	...	...	....
Periostitis, tibia	1	...	....	1	...	....
Periostitis, traumatic	1	...	....	...	...	....
Peritonitis	14	4	28.6	15	5	33.3
Pleurisy	1	...	....	...	...	....
Pleurisy, diaphragmatic	1	...	....	...	...	....
Pleurisy with effusion	1	...	....	...	...	....
Pneumonia	1	1	100.0	1	1	100.0
Poliomyelitis	2	...	....	1	...	....
Poliomyelitis, anterior	1	...	....	...	...	....
Polyp, rectum	1	...	....	...	...	....
Pott's disease	...	...	....	1	...	....
Pregnancy	...	...	....	2	...	....
Proctitis	...	...	....	2	...	....
Prolapse, rectum	8	1	12.5	5	...	....
Prolapse, sigmoid	2	...	....	...	...	....
Prostatitis	2	...	....	...	...	....
Prostate, enlarged	30	10	33.3	...	...	....
Prostate, irritable	1	...	....	...	...	....
Pyelitis	...	...	....	1	...	....
Pyonephrosis	1	...	....	...	...	....
Pyopneumothorax	2	1	50.0	...	...	....
Pyosalpinx, double	...	...	....	1	...	....
Rachitis	4	1	25.0	...	...	....
Ranula	1	...	....	2	...	....
Recklinghausen's disease	...	...	....	1	...	....
Redundant prepuce	1	...	....	...	...	....
Relaxed joints	...	...	....	1	...	....
Retention, urine	2	...	....	...	...	....
Retroflexion, uterus	...	...	....	1	...	....
Rupture, bowel	1	1	100.0	...	...	....

Table 51. Colored Surgical Cases—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Rupture, duodenum	1	1	100.0	...	...	....
Rupture, liver	1	1	100.0	...	...	....
Rupture, sphincter ani	...	...	....	1	...	....
Rupture, urethra	7	1	14.3	...	...	....
Sabre-shins	1	...	....	5	...	....
Salpingitis	...	...	....	18	...	....
Salpingo-oophoritis	...	...	....	4	2	50.0
Sarcoma, ankle	1	...	....	...	...	....
Sarcoma, breast	...	...	....	3	1	33.3
Sarcoma, cervical gland	1	...	....	...	...	....
Sarcoma, femur	2	...	....	1	...	....
Sarcoma, groin	1	...	....	...	...	....
Sarcoma, heel	2	...	....	...	...	....
Sarcoma, humerus	2	...	....	...	...	....
Sarcoma, ilium	1	...	....	...	...	....
Sarcoma, leg	1	...	....	1	...	....
Sarcoma, inferior maxilla	1	...	....	...	...	....
Sarcoma, inguinal glands	1	...	....	...	...	....
Sarcoma, maxilla	...	...	....	1	...	....
Sarcoma, neck	1	...	....	...	...	....
Sarcoma, retroperitoneal	2	1	50.0	...	...	....
Sarcoma, right superior maxilla	...	...	....	1	...	....
Sarcoma, skull	1	1	100.0	...	...	....
Sarcoma, superior maxilla	...	...	....	1	...	....
Sarcoma, thigh	...	...	....	1	...	....
Scabies	...	...	....	1	...	....
Scar	...	...	....	1	...	....
Scar, painful	...	...	....	1	...	....
Scars, contracted	1	...	....	1	...	....
Scoliosis	...	...	....	1	...	....
Separation, epiphysis	...	...	....	1	...	....
Septicæmia	2	1	50.0	...	...	....
Shock, postoperative	...	...	....	1	...	....
Sinusitis	4	...	....	...	...	....
Sinus, back	1	...	....	...	...	....
Sinus, chest	1	...	....	...	...	....
Sinuses, perineal	1	1	100.0	...	...	....
Sinus over trochanter	1	...	....	...	...	....
Solitary tubercle	1	1	100.0	...	...	....
Sprain	1	...	....	...	...	....
Sprain, back	1	...	....	...	...	....
Stomatitis	1	...	....	1	...	....
Stricture, œsophagus	5	...	....	7	1	14.3
Stricture, rectum	3	...	....	9	...	....
Stricture, urethra	34	1	2.9	...	...	....
Synovitis, knee	3	...	....	...	...	....
Syphilis	10	1	10.0	12	1	8.3
Syphilis, tertiary	...	...	....	1	...	....
Syphilitic periostitis	1	...	....	...	...	....
Syphilitic ulcer, leg	2	...	....	3	...	....
Talipes equino-varus	2	...	....	2	1	50.0
Tenosynovitis	3	...	....	2	...	....
Tetanus	10	8	80.0	...	...	....
Thrombosis	1	1	100.0	...	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

	Males.			Females.		
Causes.	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent
Thrombosis, mesenteric	1	1	100.0	...	...	....
Tonsil, enlarged	5	...	....	32	...	....
Tonsillitis	3	...	....	3	...	....
Transfusion, blood, donor of	...	...	....	1	...	....
Tubercle, brain	1	1	100.0	...	...	....
Tuberculosis, arm	...	...	....	1	...	....
Tuberculosis, axillary glands	1	...	....	...	...	....
Tuberculosis, breast	...	...	....	1	...	....
Tuberculosis, carpal bone	1	...	....	...	...	....
Tuberculosis, cæcum	1	...	....	...	...	....
Tuberculosis, cervical glands	...	...	....	2	...	....
Tuberculosis, chest wall	1	...	....	...	...	....
Tuberculosis, cutis	...	...	....	1	...	....
Tuberculosis, elbow	2	...	....	...	...	....
Tuberculosis, foot	4	...	....	1	...	....
Tuberculosis, general	1	1	100.0	...	...	....
Tuberculosis, groin	...	...	....	1	...	....
Tuberculosis, hip	7	1	14.3	2	...	....
Tuberculosis, humerus	1	...	....	...	...	....
Tuberculosis, jaw	...	...	....	1	...	....
Tuberculosis, kidney	3	1	33.3	2	...	....
Tuberculosis, os calcis	1	...	....	...	...	....
Tuberculosis, pulmonary	4	2	50.0	...	...	....
Tuberculosis, rib	3	...	....	2	...	....
Tuberculosis, sacro-iliac joint	1	...	....	1	...	....
Tuberculosis, sacrum	1	...	....	...	...	....
Tuberculosis, salivary glands	...	...	....	1	...	....
Tuberculosis, tarsus	2	...	....	3	...	....
Tuberculosis, tendon sheaths	1	...	....	...	...	....
Tuberculosis, testicle	1	...	....	...	...	....
Tuberculosis, thigh	1	...	....	...	...	....
Tuberculosis, tibia	...	...	....	1	...	....
Tuberculosis, trochanter	1	...	....	...	...	....
Tuberculosis, skull	...	...	....	1	...	....
Tuberculosis, sternum	2	...	....	2	...	....
Tuberculosis, vertebræ	50	7	14.0	11	1	9.1
Tuberculosis, wrist	1	...	....	...	...	....
Tuberculous abscess, back	...	...	....	1	...	....
Tuberculous abscess, cervical	2	...	....	2	...	....
Tuberculous abscess, chest	...	...	....	1	...	....
Tuberculous abscess, groin	1	...	....	...	...	....
Tuberculous abscess, inguinal	1	...	....	...	...	....
Tuberculous abscess, n. s.	1	...	....	...	...	....
Tuberculous adenitis, axillary	2	...	....	2	1	50.0
Tuberculous adenitis, cervical	80	1	1.3	65	...	....
Tuberculous adenitis, iliac	...	...	....	1	...	....
Tuberculous adenitis, inguinal	6	...	....	...	...	....
Tuberculous adenitis, mesenteric	3	...	....	1	...	....
Tuberculous adenitis, peritonitis	9	5	55.6	4	1	25.0
Tuberculous arthritis	24	...	....	15	1	6.7
Tuberculous arthritis, ankle	6	...	....	5	...	....
Tuberculous arthritis, elbow	8	1	12.5	2	...	....
Tuberculous arthritis, hip	6	...	....	11	1	9.1
Tuberculous arthritis, knee	14	1	7.1	2	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Tuberculous arthritis, wrist	8	2	25.0	...	...	....
Tuberculous arthritis, sacro-iliac region	1	...	....	...	...	....
Tuberculous arthritis, shoulder	1	...	....	1	...	....
Tuberculous cystitis	2	1	50.0	...	...	....
Tuberculous epididymitis	1	...	....	...	...	....
Tuberculous laryngitis	...	...	....	3	...	....
Tuberculous peritonitis	9	5	55.6	4	1	25.0
Tumor, breast	...	...	....	1	...	....
Tumor, cerebral	6	1	16.7	5	2	40.0
Tumor, fauces	1	...	....	...	...	....
Tumor, inguinal region	...	...	....	1	...	....
Tumor, parotid	2	...	....	2	...	....
Tumor, pelvic	1	...	....	...	...	....
Tumor, spermatic cord	1	...	....	...	...	....
Tumor, spinal cord	1	1	100.0	...	...	....
Ulcer, corneal	1	...	....	...	...	....
Ulcer, duodenum	...	...	....	1	...	....
Ulcer, foot	1	...	....	2	...	....
Ulcer, gastric	7	...	....	2	...	....
Ulcer, leg	2	...	....	6	1	16.7
Ulcer, leg, varicose	...	...	....	3	...	....
Ulcer, neck	1	...	....	...	...	....
Ulcer, penis	1	...	....	...	...	....
Ulcer, varicose	...	...	....	1	...	....
Uræmia	...	...	....	1	...	....
Urethritis	10	...	....	...	...	....
Varicocele	1	...	....	...	...	....
Varicose veins	8	...	....	8	...	....
Visceroptosis	...	...	....	1	...	....
Volvulus, sigmoid	1	...	....	...	...	....
Wound, abdomen, infected	...	...	....	1	...	....
Wound, abdomen, gunshot	1	...	....	...	...	....
Wound, buttocks, granulating	1	...	....	...	...	....
Wound, contused	2	...	....	2	1	50.0
Wound, face, gunshot	1	...	....	...	...	....
Wound, foot, infected	1	...	....	...	...	....
Wound, granulating	2	...	....	2	...	....
Wound, gunshot	21	3	14.3	1	...	....
Wound, incised	7	...	....	3	...	....
Wound, infected	9	...	....	5	...	....
Wound, lacerated	11	...	....	3	...	....
Wound, leg, gunshot	1	...	....	...	...	....
Wound, punctured	3	...	....	1	...	....
Wound, scalp	1	...	....	...	...	....
Wound, shoulder, gunshot	2	...	....	...	...	....
Wound, stab	12	...	....	3	...	....
Wrist-drop	1	...	....	...	...	....
Eye and ear diseases						
Cataract	5	...	....	10	...	....
Cataract, traumatic	1	...	....	...	...	....
Closed pupil	...	...	....	1	...	....
Conjunctivitis	...	...	....	2	...	....
Ectropion	...	...	....	1	...	....

TABLE 51. COLORED SURGICAL CASES—Continued.

Causes.	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
Foreign body in eye	1	...	....	...	...	....
Glaucoma	2	...	....	...	...	....
Glioma, retina	1	...	....	1	...	....
Inflamed eyeball	...	...	....	1	...	....
Irido-cyclitis	2	...	....	1	...	....
Obstruction, lachrymal duct	1	...	....	...	...	....
Occlusion, pupil	1	...	....	...	...	....
Opacity, lens	...	...	....	1	...	....
Ophthalmitis	1	...	....	...	...	....
Otitis media	1	...	....	2	...	....
Panophthalmitis	3	...	....	...	...	....
Pterygium	...	...	....	1	...	....
Rupture, cornea	2	...	....	...	...	....
Rupture, eyeball	...	...	....	1	...	....
Staphyloma, cornea	2	...	....	1	...	....
Unclassified	...	...	....	2	...	....

TABLE 52. COLORED GYNECOLOGICAL CASES.

Causes.	Admitted.	Died.	Per cent.
Abdominal pain	12	..	....
Abortion	3	..	....
Abortion, incomplete	1	..	....
Abscess, abdominal	5	1	20.0
Abscess, Bartholin's gland	7	..	....
Abscess, breast	1	..	....
Abscess, broad ligament	1	..	....
Abscess, inguinal gland	1	..	....
Abscess, ischio-rectal	9	..	....
Abscess, labial	1	..	....
Abscess, ovarian	1	..	....
Abscess, pelvic	104	6	5.8
Abscess, perirectal	1	..	....
Abscess, tubo-ovarian	20	..	....
Abscess, vagina and uterus	1	..	....
Abscess, vulvo-vaginal gland	2	..	....
Actinomycosis	1	1	100.0
Adenomyoma	1	..	....
Adenitis, inguinal	9	..	....
Adeno-carcinoma	2	1	50.0
Adhesions, intestinal	1	..	....
Adhesions, omental	1	..	....
Adhesions, postoperative	8	..	....
Amenorrhœa	9	..	....
Anemia due to menorrhagia	1	..	....
Appendicitis	40	3	7.5
Ascites	1	..	....
Atresia, vagina	4	..	....
Buboes	2	..	....
Calculus, biliary	2	1	50.0
Carcinoma, bladder	2	..	....
Carcinoma, breast	1	..	....

TABLE 52. COLORED GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Carcinoma, colon	1	..	....
Carcinoma, kidney	1	..	....
Carcinoma, ovary	2	..	....
Carcinoma, pelvic	2	..	....
Carcinoma, rectum	3	1	33.3
Carcinoma, sigmoid flexure	2	..	....
Carcinoma, stomach	1	..	....
Carcinoma, urethral	4	..	....
Carcinoma, uterus (cervix)	68	8	11.8
Carcinoma, uterus (fundus)	1	..	....
Carcinoma, uterus and ovary	1	..	....
Carcinoma, vagina	1	..	....
Carcinosis	2	..	....
Carcinosis, peritoneum	1	..	....
Caruncle, urethral	7	..	....
Cellulitis	4	..	....
Cervicitis	1	..	....
Chancroid	3	..	....
Colostomy, inguinal	1	..	....
Condylomata	1	..	....
Condylomata, vulva	1	..	....
Cyst, dermoid	2	..	....
Cyst, labial	2	..	....
Cyst, ovarian	45	..	....
Cyst, ovarian adeno-cystoma	4	1	25.0
Cyst, ovarian dermoid	1	..	....
Cyst, ovarian, Graafian follicle	2	..	....
Cyst, tubo-ovarian	1	..	....
Cystitis	29	..	....
Cystocele	1	..	....
Dysmenorrhœa	42	..	....
Dyspareunia	2	..	....
Elongated cervix	1	..	....
Endocervicitis	1	..	....
Endometritis	1	..	....
Erosion, cervix	1	..	....
Fever, typhoid	6	1	16.7
Fibroma	1	..	....
Fibroma, abdominal wall	1	..	....
Fibroma, labium	1	..	....
Fibroma, pelvis	1	..	....
Fissure in ano	2	..	....
Fistula in ano	8	1	12.5
Fistula, rectal	1	..	....
Fistula, recto-vaginal	4	..	....
Fistula, urethral	1	..	....
Fistula, urethral-vaginal	1	..	....
Fistula, vesico-vaginal	10	2	20.0
Foreign body in bladder	1	..	....
Foreign body in vagina	1	..	....
Gastritis	1	1	100.0
Gonorrheal peritonitis	1	..	....
Hematocele, pelvic	1	..	....
Hematuria	4	..	....

TABLE 52. COLORED GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Hemorrhage	1	..	....
Hemorrhage, post-partum	1	..	....
Hemorrhage, uterine	5	..	....
Hemorrhoids	11	1	9.1
Hernia, femoral	2	..	....
Hernia, inguinal	2	..	....
Hernia, inguinal, left	1	..	....
Hernia, inguinal, right	1	..	....
Hernia, postoperative	1	..	....
Hernia, umbilical	3	..	....
Hernia, ventral	13	..	....
Hydrocele	4	..	....
Hydrosalpinx	4	..	....
Hypernephroma	2	1	50.0
Hypertrophy, cervix	8	..	....
Hypertrophy, labium	1	..	....
Hypertrophy, labia majora	1	..	....
Hypertrophy, vaginal wall	1	..	....
Hysteria	1	..	....
Incontinence, urine	3	..	....
Infantile pelvic organs	1	..	....
Intestinal obstruction	6	3	50.0
Irregular menstruation	1	..	....
Laceration, cervix	3	..	....
Laceration, para-urethral	1	..	....
Leucorrhœa	6	..	....
Menopause, artificial	1	..	....
Metrorrhagia	34	..	....
Myoma, uterus	464	18	3.9
Nephritis	1	..	....
Nephroptosis	2	..	....
Neurasthenia	2	..	....
Papillocystoma, ovary	1	1	100.0
Papilloma, ovary	1	..	....
Pelvic inflammatory disease	13	..	....
Perineal tear	1	..	....
Peritonitis	48	5	10.4
Peritonitis, general	3	1	33.3
Peritonitis, pelvic	4	..	....
Peritonitis, plastic	1	..	....
Periureteritis	1	..	....
Pneumonia	1	..	....
Polyp, cervical	1	..	....
Pregnancy	38	..	....
Pregnancy, extra-uterine	54	2	3.7
Proctitis	4	..	....
Prolapse, vagina	1	..	....
Pseudocyesis	1	..	....
Pyelitis	4	..	....
Pyonephrosis	5	..	....
Pyosalpinx	46	2	4.3
Relaxed sacro-iliac joint	1	..	....
Relaxed vaginal outlet	33	..	....
Retained secundines	30	..	....

TABLE 52. COLORED GYNECOLOGICAL CASES—Continued.

Causes.	Admitted.	Died.	Per cent.
Retention, urine	1	..	....
Salpingitis	2	..	....
Salpingo-oophoritis	681	3	0.4
Sarcoma, canal of neck	1	..	....
Sarcoma, kidney	1	..	....
Sarcoma, ovary	1	..	....
Sarcoma, uterus	2	1	50.0
Septicæmia, puerperal	3	..	....
Sinus, abdominal	2	..	....
Sinus, postoperative	1	..	....
Sterility	3	..	....
Stricture, rectum	27	1	3.7
Stricture, ureteral	2	1	50.0
Syphilis	1	..	....
Syphilitic condylomata	1	..	....
Tear, recto-vaginal septum	7	..	....
Tuberculosis, bladder	1	..	....
Tuberculosis, intestinal	2	..	....
Tuberculosis, kidney	2	..	....
Tuberculosis, pelvic organs	4	..	....
Tuberculosis, pulmonary	2	..	....
Tuberculosis, retroperitoneal	1	..	....
Tuberculosis, sacro-iliac region	1	..	....
Tuberculosis, tubes	2	..	....
Tuberculous peritonitis	7	..	....
Tuberculous pleurisy	1	..	....
Tumor, rectal	1	..	....
Ulcer, vagina	2	..	....
Ulcer, vulva	2	..	....
Urethritis	5	..	....
Urethritis and vaginitis	1	..	....
Uterus, anteflexion	2	..	....
Uterus, collapse	24	..	....
Uterus, descensus	1	..	....
Uterus, inversion	1	..	....
Uterus, retroposition	71	..	....
Uterus, subinvoluted	2	..	....
Vaginitis	1	..	....
Vulvitis	2	..	....
Vulvo-vaginitis	1	..	....
*Unclassified	88	..	....

* Includes cases of doubtful terminology.

TABLE 53. SUMMARY OF COLORED OBSTETRICAL CASES FOR THE PERIOD 1904-1911.

Causes.	Admitted.	Died.	Per cent.
Labor, spontaneous, at term	957	1	0.1
Labor, spontaneous, premature	74	2	2.7
Labor, operative	173	12	6.9
Abortion	89	1	1.1
Admitted post-partum	21	6	28.6
Pregnant, not delivered	110	0	0.0
Not pregnant	9	0	0.0
Total	1433	22	1.5

Causes.	Admitted.		Died.	
	Number.	Per cent.	Number.	Per cent.
Labor, spontaneous at term	957	66.8	1	4.5
Labor, spontaneous, premature	74	5.1	2	9.1
Labor, operative	173	12.1	12	54.6
Abortion	89	6.2	1	4.5
Admitted post-partum	21	1.5	6	27.3
Pregnant, not delivered	110	7.7	0	0.0
Not pregnant	9	0.6	0	0.0
Total	1433	100.0	22	100.0

SEC. G. SUPPLEMENTARY AND MISCELLANEOUS STATISTICS.

TABLE 54. ADMISSION RATE OF WHITE CASES OF MALIGNANT TUMORS.

	Males.		Females.	
	Malignant tumors.	Rate per 10,000 population.	Malignant tumors.	Rate per 10,000 population.
1892	58	3.2	79	4.0
1893	46	2.5	99	5.0
1894	50	2.6	131	6.5
1895	77	4.0	123	6.0
1896	99	5.1	122	5.8
1897	95	4.8	105	5.0
1898	82	4.1	168	7.8
1899	94	4.6	123	5.6
1900	95	4.6	141	6.4
1901	104	5.0	120	5.4
1902	92	4.3	112	5.0
1903	97	4.5	108	4.7
1904	117	5.4	110	4.8
1905	108	4.9	91	3.9
1906	103	4.7	82	3.5
1907	99	4.4	105	4.4
1908	119	5.3	108	4.5
1909	104	4.6	89	3.7
1910	117	5.1	106	4.3
1911	103	4.5	70	2.8
1892-01	800	4.1	1211	5.8
1902-11	1059	4.8	981	4.2

TABLE 55. ADMISSION RATE OF COLORED CASES OF MALIGNANT TUMORS.

	Males.		Females.	
	Malignant tumors.	Rate per 10,000 population.	Malignant tumors.	Rate per 10,000 population.
1892	3	1.0	11	2.8
1893	7	2.3	7	1.8
1894	3	1.0	22	5.4
1895	14	4.3	24	5.8
1896	9	2.7	11	2.6
1897	4	1.2	11	2.6
1898	13	3.8	17	4.0
1899	12	3.4	23	5.3
1900	7	2.0	19	4.3
1901	4	1.1	26	5.9
1902	5	1.4	14	3.2
1903	13	3.6	10	2.2
1904	8	2.2	18	4.0
1905	17	4.6	17	3.8
1906	14	3.7	20	4.4
1907	5	1.3	29	6.4
1908	20	5.2	16	3.5
1909	10	2.6	24	5.3
1910	9	2.3	24	5.3
1911	18	4.6	31	6.8
1892-01	76	2.3	171	4.1
1902-11	119	3.2	203	4.5

TABLE 56. WHITE CASES OF MALIGNANT TUMORS.

	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
1892	58	5	8.6	79	8	10.1
1893	46	11	23.9	99	14	14.1
1894	50	10	20.0	131	15	11.5
1895	77	15	19.5	123	14	11.4
1896	99	14	14.1	122	14	11.5
1897	95	18	18.9	105	9	8.6
1898	82	10	12.2	168	20	11.9
1899	94	13	13.8	123	9	7.3
1900	95	7	7.4	141	15	10.6
1901	104	20	19.2	120	12	10.0
1902	92	18	19.6	112	21	18.8
1903	97	17	17.5	108	11	10.2
1904	117	16	13.7	110	14	12.7
1905	108	19	17.6	91	11	12.1
1906	103	14	13.6	82	7	8.5
1907	99	12	12.1	105	13	12.4
1908	119	18	15.1	108	6	5.6
1909	104	8	7.7	89	5	5.6
1910	117	15	12.8	106	13	12.3
1911	103	22	21.4	70	4	5.7
1892-01	800	123	15.4	1211	130	10.7
1902-11	1059	159	15.0	981	105	10.7

Table 57. Colored Cases of Malignant Tumors.

	Males.			Females.		
	Admitted.	Died.	Per cent.	Admitted.	Died.	Per cent.
1892	3	1	33.3	11	4	36.4
1893	7	2	28.6	7	..	....
1894	3	2	66.7	22	2	9.1
1895	14	3	21.4	24	5	20.8
1896	9	1	11.1	11	4	36.4
1897	4	..	....	11	..	....
1898	13	2	15.4	17	3	17.6
1899	12	3	25.0	23	5	21.7
1900	7	1	14.3	19	4	21.1
1901	4	2	50.0	26	5	19.2
1902	5	2	40.0	14	3	21.4
1903	13	2	15.4	10	2	20.0
1904	8	5	62.5	18	2	11.1
1905	17	4	23.5	17	2	11.8
1906	14	8	57.1	20	5	25.0
1907	5	1	20.0	29	..	....
1908	20	3	15.0	16	2	12.5
1909	10	2	20.0	24	4	16.7
1910	9	1	11.1	24	2	8.3
1911	18	3	16.7	31	1	3.2
1892-01	76	17	22.4	171	32	18.7
1902-11	119	31	26.1	203	23	11.3

Table 58. Population of Baltimore, Md., 1892-1911.

	White males.	White females.	Colored males.	Colored females.
1892	183107	196448	30437	39345
1893	186187	199575	31074	39952
1894	189267	202703	31711	40559
1895	192347	205831	32348	41166
1896	195427	208959	32985	41774
1897	198507	212087	33622	42382
1898	201587	215215	34259	42990
1899	204667	218343	34896	43598
1900	208217	221482	35063	44195
1901	210309	223793	35462	44345
1902	212401	226104	35861	44495
1903	214493	228415	36260	44645
1904	216585	230726	36659	44795
1905	218677	233037	37058	44945
1906	220769	235348	37457	45095
1907	222862	237659	37856	45245
1908	224955	239971	38255	45395
1909	227048	242283	38654	45545
1910	229141	244595	39054	45695
1911	231234	246907	39454	45845
1892-01..........	1969622	2104436	331857	420306
1902-11..........	2218165	2365045	376568	451700

TABLE 59. DEATHS BY SEX AND COLOR IN BALTIMORE, MD., 1902-1911.

	Deaths.	Rate per 1000 population.
White males	41904	18.9
White females	39504	16.7
Total white	81408	17.8
Colored males	13352	35.3
Colored females	13058	28.9
Total colored	26410	31.8

TABLE 60. DEATHS IN BALTIMORE, MD., 1907-1911.

	Pulmonary tuberculosis.		Pneumonia.	
	Deaths.	Rate per 10,000 population.	Deaths.	Rate per 10,000 population.
White males	2292	20.2	1807	15.9
White females	1700	14.0	1684	13.9
Total white	3992	17.0	3491	14.9
Colored males	1164	60.2	986	51.0
Colored females	1016	44.6	846	37.2
Total colored	2180	51.8	1832	43.5

	Bronchitis.		Typhoid fever.	
	Deaths.	Rate per 10,000 population.	Deaths.	Rate per 10,000 population.
White males	256	2.3	443	3.9
White females	330	2.7	312	2.6
Total white	586	2.5	755	3.2
Colored males	86	4.4	102	5.3
Colored females	118	5.2	78	3.4
Total colored	204	4.8	180	4.3

	Cancer.		Heart disease.	
	Deaths.	Rate per 10,000 population.	Deaths.	Rate per 10,000 population.
White males	725	6.4	1561	13.8
White females	1217	10.1	1650	13.6
Total white	1942	8.3	3211	13.7
Colored males	71	3.7	600	31.0
Colored females	202	8.9	562	24.7
Total colored	273	6.5	1162	27.6

	Bright's Disease.		Accident.		Suicide.	
	Deaths.	Rate per 10,000 population.	Deaths.	Rate per 10,000 population.	Deaths.	Rate per 10,000 population.
Whites	3677	15.7	1987	8.5	441	1.9
Colored	1075	25.5	575	13.7	24	0.6

TABLE 61. PATIENTS TREATED AND DAYS OF TREATMENT.

	Treated.	Days of treatment.	Average number of days.
1892	2253	61772	27.4
1893	2622	68044	26.0
1894	3018	76386	25.3
1895	3386	86289	25.5
1896	3602	88690	24.6
1897	3633	87993	24.2
1898	3815	92701	24.3
1899	4074	96116	23.6
1900	4702	100128	21.3
1901	4363	101763	23.3
1902	4164	103343	24.8
1903	4166	100879	24.2
1904	4531	109923	24.3
1905	4224	100906	23.9
1906	4550	101178	22.2
1907	4859	103778	21.4
1908	4912	102208	20.8
1909	5085	104654	20.6
1910	5267	112150	21.3
1911	5199	100165	19.3
1892-01	35468	859882	24.2
1902-11	46957	1039184	22.1

TABLE 62. THE DISPENSARY.

	Medical Department.		Surgical Department.	
	Number.	Per cent.	Number.	Per cent.
1892	11967	24.5	9759	20.0
1893	13920	25.0	9929	17.9
1894	14808	26.4	9905	17.6
1895	13755	25.0	10047	18.2
1896	16069	25.6	11104	17.7
1897	16613	25.9	11237	17.5
1898	15199	24.9	11550	18.9
1899	14638	24.6	11862	19.9
1900	15561	23.7	14229	21.7
1901	14070	22.1	13715	21.5
1902	14489	23.4	11450	18.5
1903	14660	23.0	12938	20.3
1904	14097	22.0	13118	20.4
1905	16100	22.5	14255	20.0
1906	12976	19.1	14255	21.0
1907	15654	20.9	13088	17.4
1908	15543	18.6	14632	17.5
1909	13872	17.6	14681	18.6
1910	15658	18.8	13580	16.3
1911	12656	17.9	11819	16.7
1892-01	146600	24.7	113337	19.1
1902-11	145705	20.2	133816	18.6

Table 63. The Dispensary.

	Gynecological Department.		Obstetrical Department.	
	Number.	Per cent.	Number.	Per cent.
1892	3415	7.0	....	..
1893	4678	8.4	....	..
1894	3760	6.7	9	..
1895	4017	7.3	369	0.7
1896	4179	6.7	594	0.9
1897	3959	6.2	593	0.9
1898	3055	5.0	758	1.2
1899	3531	5.9	745	1.3
1900	3127	4.8	1124	1.7
1901	2504	3.9	1025	1.6
1902	2398	3.9	1336	2.2
1903	2626	4.1	1385	2.2
1904	2761	4.3	1420	2.2
1905	3376	4.7	1431	2.0
1906	3491	5.1	1373	2.0
1907	4047	5.4	1904	2.5
1908	4046	4.9	2061	2.5
1909	3781	4.8	2005	2.5
1910	4630	5.6	2167	2.6
1911	3981	5.6	1925	2.7
1892-01	36225	6.1	5217	0.9
1902-11	35137	4.9	17007	2.4

Table 64. The Dispensary.

	Children's Department.		Orthopedic Department.	
	Number.	Per cent.	Number.	Per cent.
1892	2407	4.9	....	..
1893	2440	4.4	....	..
1894	2646	4.7	....	..
1895	2288	4.2	....	..
1896	2983	4.8	....	..
1897	3041	4.7	....	..
1898	2723	4.5	....	..
1899	2131	3.6	....	..
1900	2732	4.2	....	..
1901	2707	4.3	323	0.5
1902	2808	4.5	1902	3.1
1903	2409	3.8	2235	3.5
1904	2563	4.0	3006	4.7
1905	2913	4.1	3416	4.8
1906	2556	3.8	2718	4.0
1907	3495	4.7	2157	2.9
1908	3770	4.5	2615	3.1
1909	3802	4.8	2354	3.0
1910	4763	5.7	2341	2.8
1911	3642	5.2	2426	3.4
1892-01	26098	4.4	323	0.1
1902-11	32721	4.5	25170	3.5

TABLE 65. THE DISPENSARY.

	Dermatological Department.		Department of Venereal Diseases.[1]	
	Number.	Per cent.	Number.	Per cent.
1892	4520	9.3	....	..
1893	5352	9.6	....	..
1894	5182	9.2	....	..
1895	4765	8.6	....	..
1896	5174	8.3	....	..
1897	5229	8.1	794	1.2
1898	5551	9.1	1283	2.1
1899	6117	10.3	1239	2.1
1900	5929	9.0	1683	2.6
1901	5641	8.9	1473	2.3
1902	5150	8.3	1374	2.2
1903	4439	6.9	1416	2.2
1904	5061	7.9	933	1.5
1905	5086	7.1	1222	1.7
1906	5058	7.5	947	1.4
1907	5226	7.0	1312	1.7
1908	5186	6.2	1241	1.5
1909	4695	6.0	1290	1.6
1910	5245	6.3	1284	1.5
1911	5035	7.1	1119	1.6
1892-01	53460	9.0	6472	1.1
1902-11	50181	7.0	12138	1.7

From 1907 this department is indicated as Women's Venereal.

TABLE 66. THE DISPENSARY.

	Ophthalmological Department.		Otological Department.	
	Number.	Per cent.	Number.	Per cent.
1892	1977	4.0	772	1.6
1893	2514	4.5	928	1.7
1894	2653	4.7	951	1.7
1895	2812	5.1	854	1.5
1896	4065	6.5	1253	2.0
1897	4398	6.8	1298	2.0
1898	3402	5.6	1087	1.8
1899	2896	4.9	1147	1.9
1900	3659	5.6	1474	2.2
1901	3510	5.5	1339	2.1
1902	3520	5.7	1035	1.7
1903	3523	5.5	1009	1.6
1904	3031	4.7	1151	1.8
1905	3449	4.8	1131	1.6
1906	3336	4.9	922	1.4
1907	3326	4.4	1264	1.7
1908	3331	4.0	1496	1.8
1909	3581	4.5	1159	1.5
1910	4092	4.9	1414	1.7
1911	3385	4.8	1038	1.5
1892-01	31886	5.4	11103	1.9
1902-11	34574	4.8	11619	1.6

Table 67. The Dispensary.

	Genito-urinary Department.		Laryngological Department.	
	Number.	Per cent.	Number.	Per cent.
1892	3847	7.9	4122	8.4
1893	3865	7.0	4437	8.0
1894	4962	8.8	4913	8.8
1895	4393	8.0	4536	8.2
1896	4583	7.3	5068	8.1
1897	5247	8.2	4712	7.3
1898	6210	10.2	3461	5.7
1899	4989	8.4	3268	5.5
1900	5808	8.9	3821	5.8
1901	6715	10.5	3476	5.5
1902	6725	10.9	3027	4.9
1903	6838	10.7	3454	5.4
1904	7755	12.1	3080	4.8
1905	8200	11.5	3110	4.4
1906	9439	13.9	3349	4.9
1907	9503	12.7	3851	5.1
1908	9126	10.9	4499	5.4
1909	8724	11.1	4281	5.4
1910	8383	10.1	4279	5.1
1911	6600	9.3	3436	4.9
1892-01	50619	8.5	41814	7.1
1902-11	81293	11.3	36366	5.0

Table 68. The Dispensary.

	Neurological Department.		Admitted to Hospital.	
	Number.	Per cent.	Number.	Per cent.
1892	5627	11.5	420	0.9
1893	7135	12.8	376	0.7
1894	5660	10.1	730	1.3
1895	6600	12.0	661	1.2
1896	7115	11.3	531	0.8
1897	6731	10.5	421	0.7
1898	6498	10.6	255	0.4
1899	6925	11.6	18	..
1900	6430	9.8	...	..
1901	7171	11.3	...	..
1902	6629	10.7	...	..
1903	6907	10.8	...	..
1904	6196	9.6	...	..
1905	7746	10.8	...	..
1906	6608	9.8	...	..
1907	7156	9.5	...	..
1908	7215	8.6	...	..
1909	6745	8.6	...	..
1910	7063	8.5	...	..
1911	6298	8.9	...	..
1892-01	65892	11.1	3412	0.6
1902-11	68563	9.5	...	..

TABLE 69. THE DISPENSARY

	Total Number treated.	Phipps' Tuberculosis Dispensary.	
		Number.	Per cent.
1892	48833	....	...
1893	55574	....	...
1894	56179	....	...
1895	55097	....	...
1896	62718	....	...
1897	64273	....	...
1898	61032	....	...
1899	59506	....	...
1900	65577	....	...
1901	63669	....	...
1902	61843	....	...
1903	63839	....	...
1904	64172	....	...
1905	71435	....	...
1906	67861	833	1.2
1907	75021	3038	4.1
1908	83567	8806	10.5
1909	78849	7879	10.0
1910	83347	8448	10.1
1911	70740	7380	10.4
1892-01	592458	....	...
1902-11	720674	36384	5.0

TABLE 70. THE DISPENSARY.

(1892-1901.)

Department.	Treated.	Per cent.
Medicine	146600	24.7
Surgery	113337	19.1
Neurology	65892	11.1
Dermatology	53460	9.0
Genito-urinary	50619	8.5
Laryngology	41814	7.1
Gynecology	36225	6.1
Ophthalmology	31886	5.4
Children	26098	4.4
Otology	11103	1.9
Venereal [1]	6472	1.1
Obstetrical [2]	5217	0.9
Admitted to Hospital [3]	3412	0.6
Orthopedic [4]	323	0.1
Total	592458	100.0

[1] From 1897 only.
[2] From 1894 only.
[3] From 1892 to 1899 only.
[4] From 1901 only.

TABLE 70. THE DISPENSARY—Continued.
(1902-1911.)

Department.	Treated.	Per cent.
Medicine	145705	20.2
Surgery	133816	18.6
Genito-urinary	81293	11.3
Neurology	68563	9.5
Dermatology	50181	7.0
Phipps' Tuberculosis Dispensary[5]	36384	5.0
Laryngology	36366	5.0
Gynecology	35137	4.9
Ophthalmology	34574	4.8
Children	32721	4.5
Orthopedic	25170	3.5
Obstetrical	17007	2.4
Venereal[6]	12138	1.7
Otology	11619	1.6
Total	720674	100.0

[5] For 1906 to 1911 only. During this period the number of treated cases in the Phipp's Tuberculosis Dispensary was 7.9 per cent of all treated.

[6] From 1907 this department is indicated as Women's Venereal.

MORBIDITY AND MORTALITY STATISTICS OF THE JOHNS HOPKINS HOSPITAL, 1903-1911.

TABLE 71. X-RAY DEPARTMENT.

	Cases treated.	Treatments given.	Per cent of increase or decrease.
1903	114	1461	......
1904	101	1086	—25.7
1905	65	901	—17.0
1906	56	687	—23.8
1907	63	768	+11.8
1908	44	566	—26.3
1909	33	490	—13.4
1910	N. S.	731	+49.2
1911	N. S.	592	—19.0
1903-11	476	7282	......

RADIOGRAPHS.

	Number.	Per cent of increase or decrease.	Ward patients.	Dispensary patients.	Orthopedic.	Private.
1903	1599	.....	752	408	183	256
1904	1394	—12.8	654	455	152	133
1905	905	—35.1	418	323	157	7
1906	822	— 9.2	405	289	124	4
1907	909	+10.6	471	334	100	4
1908	1064	+17.1	508	380	176	N. S.
1909	1401	+31.7	717	557	127	N. S.
1910	2484	+77.3	1354	954	176	N. S.
1911	4448	+79.1	2597	1851	N. S.	N. S.
1903-11	15026	.....	7876	5551	1195	404

Table 71—Continued.

FLUOROSCOPIC EXAMINATIONS.

	Number.	Per cent of increase or decrease.
1903	26	......
1904	57	+119.2
1905	162	+184.2
1906	175	+ 8.0
1907	161	— 8.0
1908	177	+ 9.9
1909	69	— 61.0
1910	84	+ 21.7
1911	84	......
1903-11	995	......

Table 72.

Financial Statistics of The Johns Hopkins Hospital, 1889-1911.

Year.	Expenditures.	Receipts.	Net cost.	No. of patients treated.	Cost per patient treated.
1899*	$ 76,085.51	$ 7,532.90	$ 68,552.61	788	$96.56
1890	139,634.77	31,236.19	108,398.58	1825	76.51
1891	154,992.87	42,156.16	112,836.71	2276	68.10
1892	161,858.29	51,162.67	110,695.62	2077	77.93
1893	172,895.42	50,499.74	122,395.68	2622	65.94
1894	178,107.11	52,012.28	126,094.83	3018	59.01
1895	188,868.83	61,168.82	127,700.01	3386	55.78
1896	191,111.74	61,635.68	129,476.06	3602	53.06
1897	200,963.72	64,391.71	136,572.01	3633	55.32
1898	198,643.78	66,530.57	132,113.21	3815	52.07
1899	214,113.63	87,756.60	126,357.03	4074	52.56
1900	228,870.18	92,913.72	135,956.46	4702	48.68
1901	229,018.42	98,065.60	130,952.82	4363	52.49
1902	245,335.31	104,627.75	140,707.56	4164	58.92
1903	249,770.77	101,511.74	148,259.03	4166	59.95
1904	269,327.25	115,242.42	154,084.83	4531	59.44
1905	273,547.21	126,702.22	146,844.99	4224	64.76
1906	271,400.52	144,359.78	127,040.74	4550	59.65
1907	299,182.64	168,653.63	130,529.01	4859	61.57
1908	318,177.84	178,764.79	139,413.05	4912	64.78
1909	338,218.09	190,232.85	147,985.24	5085	66.51
1910	358,514.81	204,838.86	153,675.95	5267	68.07
1911	361,155.54	192,355.32	168,800.22	5199	69.47

* Eight and a half months.

THE ORIGIN AND DEVELOPMENT OF THE LYMPHATIC SYSTEM.[1]

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I. INTRODUCTION.

1. MORPHOLOGY OF THE VASCULAR SYSTEM, THE ANGIOBLAST.

Until the past few years our knowledge of the morphology of the lymphatic system was in a very unsatisfactory state. Our conceptions of such main questions as the origin of the first lymphatics, the time of their appearance, the relations of the lymph hearts and sacs of the amphibia to the lymph glands and ducts of higher forms, the relation of the lymphatics to serous cavities and to the various forms of tissue spaces, and the development of the lymphatic vessels within an organ have been so vaguely understood that the opinions of no two investigators approached agreement.

A clear conception of any system must be based on an understanding of its fundamental morphology, as, for example, the morphology of the arterial system was placed upon a satisfactory basis by the discovery and comparison of the aortic arches in different animals. An example more closely in touch with our knowledge of the lymphatic system is the study of the fundamental morphology of the blood vascular system. Our knowledge of this is in the process of being built up, but a foundation has been laid for the clear understanding of the vascular system in a series of discoveries. The first and most fundamental of these is that the blood vessels arise as blood islands in the extraembryonal membranes. The earlier embryologists on the other hand believed that the first vessels were spaces without walls, which the pressure of the circulating blood hollowed out. The best description of the

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[1] Aided by a grant from the Baltimore Association for the Promotion of University Education of Women and by the Carnegie Institution of Washington.

origin of blood islands and the best analysis of the meaning of this discovery is to be found in two works of His, "Untersuchungen ueber die erste Anlage des Wirbeltierleibes" in 1868 (pp. 95-103) and in "Lecithoblast und Angioblast" in 1900 (pp. 268-295). The discovery of blood islands, however, dates back to the work of Wolff (154) and Pander (101), who introduced the name, and perhaps no one subject in embryology has a more extensive literature. Certainly a most interesting account of the development of the vascular problem can be followed through the pages of von Baer (7), Prévost and Lebert (108), Remak (124-125), Reichert (121-123), Koelliker (67-71) and Thoma (148). The second great advance was the discovery that blood vessels throughout are lined by endothelium (Hoyer 48), which followed soon after the corresponding discovery in lymphatics by von Recklinghausen. The third discovery involves the proof that blood vessels grow by the sprouting of their endothelium, Prévost and Lebert (108), His (47), Rouget (126) and Arnold (5); the fourth that the main vessels of the body wall, including the posterior part of the aorta (Evans 33-35), even the anterior part of the aorta and lateral heart anlagen, arise as a capillary plexus or as solid angioblast cords (Bremer 15), which invade the body from the extraembryonal membranes. Finally a complete conception of the development of the vascular system is based on the theory that the blood vessels of the extraembryonal membranes invade the body wall (His 47), and that within the body wall these capillaries of endothelium gradually invade or spread over the body so that there are definite vascular and non-vascular layers and zones. His (47) discovered the fact that blood vessels grow into the central nervous system; but the theory of vascular and non-vascular zones which is essential to an understanding of the development of the vascular system we owe to Mall (80-87). It has been worked out by his pupils, notably Evans (33-35). Its meaning can be grasped by studying figs. 4, 5 and 6 in connection with fig. 437 (Evans 35), which all show that the skin dorsal to the central nervous system is a non-vascular zone, which for a long time is not reached by the blood vessels in the centrifugal growth.

This series of discoveries, notwithstanding the gaps and uncertainties in our knowledge of the early stages which were well brought out by Minot (98, pp. 483-485) and by Evans (35, pp. 551-567) in 1911, uncertainties in part since removed by the work of

Bremer (15), offers a consistent as well as a constructive theory of the vascular system which goes far to modify the force of the following words of Koelliker quoted by Rückert and Mollier (128, p. 1019): "Ueber die erste Bildung der Gefässe und des Blutes herrschen wohl ebenso viele Ansichten, als Forscher sich ueber diesen Gegenstand ausgesprochen haben, was auf jeden Fall beweist, dass derselbe zu den schwierigsten gehört." The theory thus outlined is that the fundamental morphology of the vascular system is based on the specificity of the endothelium, or in the words of His (47, p. 325), on the fact "Zu den am frühesten sich sondernden Gewebsanlagen gehört der Gefässkeim oder Angioblast. Seine Sonderung erfolgt sehr scharf, und sein Wachsthum geht nach durchaus eigenthümlichen Gesetzen vor sich." It includes the discovery of Mall (83-87) that endothelium may produce reticulum, a process which he has shown takes place both in the liver and in the heart; but maintains that there is an early differentiation of two tissues, namely, endothelium and mesenchyme, so that the angioblasts once formed give rise to all the vascular endothelium of the body.

The opposing theories in the varying forms of the origin of blood vessels from tissue spaces, their growth by the addition of tissue spaces or by the addition of connective tissue cells, and the differentiation of endothelium from mesenchyme over extensive areas within the body wall find their most recent evidence in the works of Rückert (127), Rückert and Mollier (128), Hahn (40), Bonnet (14) and Maximow, 1909 (90, p. 511). These views, however, must be traced through the earlier works of Götte (37) and Reichert (121-123). The evidence for the continued origin of blood vessels from the mesenchyme is for the most part from the interpretation of appearances in sections. Hahn's work, however, in connection with the difficult point of the origin of the heart and aorta is experimental. He removed the vascular membranes on one side of early chick embryos and obtained a heart anlage and aorta on both sides. He thought that he could entirely exclude a growth from one side to the other as well as remnants of the membranes on the same side and concluded that both heart and aorta arise in situ from the mesenchyme and not from the endoderm of the yolk sac not from an ingrowth from the extraembryonal membranes.

2. MORPHOLOGY OF THE LYMPHATIC SYSTEM.

It will be proved in the following pages that the lymphatic problem is closely connected with, or rather is a fundamental part of, the vascular problem, so that the study of the one throws light on the other, or, to put it more strongly, that the same kind of evidence is needed to solve both problems. The fundamental morphology of the lymphatic system has, however, been put on a more satisfactory basis than that of the vascular system, for it has been seen in the living embryo that the first lymphatics bud off from the veins. Moreover, lymphatics begin at a comparatively late stage, long after the formation of the blood islands has ceased.

II. HISTORICAL.

1. VASA SEROSA.

Until the primary origin of any system is known our conceptions of it are necessarily hazy and vague and this is nowhere better illustrated than in connection with the lymphatic system. The views of the eighteenth century may well be summed up in the hypothetical "vasa serosa" of Boerhave (13), Haller (41) and others, which were tiny channels too small to allow corpuscles to pass, supposed to connect arteries, veins and lymphatics at their tips. The conception which underlies vasa serosa may be traced back to the experiments of Nuck (100), who injected air into the arteries and found it returning in the lymphatics, as may be represented in the diagram of fig. 1. Vasa serosa meant the idea that the arteries finally branched into vessels too tiny to carry the corpuscles, but the term likewise represents a whole series of vague conceptions, such as Bichat's (12) absorbents and exhalants, which sought to make definite some idea of the nature of lymphatics.

2. LYMPHATICS WITH OPEN MOUTHS.

In the latter half of the eighteenth century the conception of definite "vasa serosa" was modified through the work of William Hunter (50) and Munro, who believed that lymphatics began with open mouths. The views of these English observers, as shown by Cruikshank (23), involved the idea that the mouths of the lymphatics opened directly onto the surface of the body, into the cavity of the intestine and the air sacs of the lungs, as well as into the connective tissues. The theory was also involved with discussions of the lymphatics as the exclusive organs of absorption for the body, and the physiological theories of filtration.

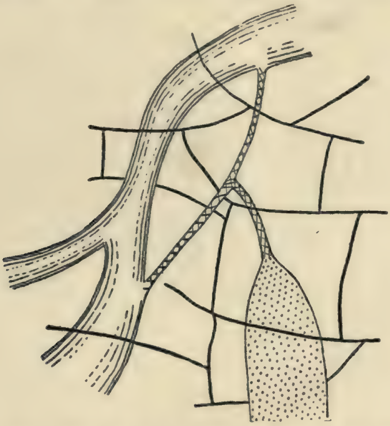

FIG. 1.—Diagram to show the "vast serosa" of Boerhave, Haller and others. The veins are striped, the lymphatics are dotted, and the "vasa serosa" which connect them are cross-hatched. The connective tissue is indicated by lines.

The doctrine, or as His (44) terms it, "the dogma of lymphatics with open mouths," was first combated by a definite counter theory by Schwann (139), following his discovery of the cell in the animal body. The theory of Schwann and notably of Virchow (150) was that in place of vasa serosa and hypothetical connections which did not exist hollow connective tissue cells spanned the gaps between blood vessels and lymphatics, fig. 2.

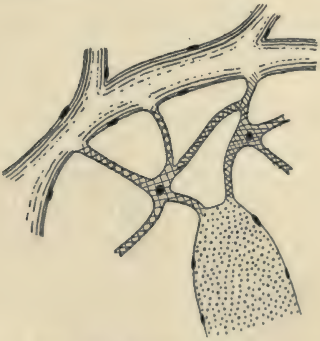

FIG. 2.—Diagram to show the theory of Schwann and of Virchow that the blood vessels are connected with lymphatics by hollow connective tissue cells. The veins are striped, the lymphatics dotted and the hypothetical lymph vessels are cross-hatched. The nuclei denote the fact that cells have been discovered.

3. DISCOVERY OF ENDOTHELIUM.

In contrast to these hypothetical relationships of lymphatics, the work of von Recklinghausen (119) gave the first definite theory which was actually based on the interpretation of direct observations of the lymphatic capillary. Through the use of silver nitrate solutions reduced in direct sunlight, he discovered that the lymphatics are lined by a definite cell layer of endothelium. This is clearly one of the most important discoveries in histology. Von Recklinghausen interpreted the silver pictures to mean that the finest lymphatic capillaries were lined by an epithelium, but that these capillaries communicated by wide openings with *Saftcanäle* or lymph radicles, which formed the real rootlets of the lymphatics. Subsequently he described more definite openings or stomata in the serosa of the diaphragm (120).

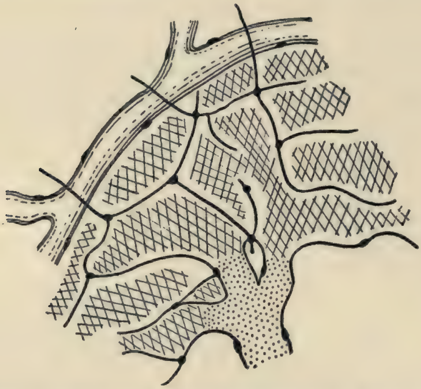

FIG. 3.—Diagram to show von Recklinghausen's theory of the relation of lymphatics to tissue spaces. All of the tissue spaces are cross-hatched to indicate hypothetical lymphatics.

The von Recklinghausen figures seemed to offer a perfectly satisfactory demonstration of the relations of open lymphatics, especially in view of the fact that the great majority of anatomists already believed in open lymphatics. But it is of great interest to follow the writings of His at this period. His (44), who was just publishing in favor of open lymphatics, and saw von Recklinghausen's paper as his own was going to press, at first recognized in von Recklinghausen's descriptions a confirmation of his own views. On careful studying of the silver pictures, however, His (45) saw that the discovery of endothelium was the very step which, instead of proving that lymphatics are open and without definite limits, tended rather to throw the balance of proof in the opposite direction; that the discovery of endothelium gave the conception of lymphatic capillaries not as indefinite spaces without walls, but as limited by a definite membrane. To quote his words (45, pp. 457-458), "Wenn ich nach den eben gemachten Auseinandersetzungen der einen Aufstellung v. Recklinghausen's, nämlich derjenigen vom Vorkommen eines Epithels in den feineren Lymphgefässen des Diaphragma vollkommen beistimme, so bin ich durchaus anderer Ansicht als jener Autor hinsichtlich der Saftcanälchen und ihrer Beziehung zu den Lymphgefässen; fürs erste nämlich leugne ich das Vorkommen von Saftcanälchen in dem Sinn von v. Recklinghausen, und zweitens halte ich die Verbindung der von ihm als Saftcanälchen gedeuteten Theile mit den Lymphgefässen nur für eine scheinbare," and later in his interpretation of the silver picture he says: "Je dünner und blasser die supervasculäre Schicht ist, um so leichter wird es den Anschein haben, als ob die hellen Figuren der intervasculären Bindegewebskörper unmittelbar in die Lymphgefässe selbst einmünden, um so eher wird man uebersehen, dass in Wirklichkeit der Zusammenhang jener Figuren nicht mit den Gefässen, sondern mit den Gefässen ueberlagerten verzweigten Körpern stattfindet." Further he adds that if the openings pictured by von Recklinghausen exist, there would be no reason why any injection of a finely divided mass should not fill practically all of the *Saftcanälchen* or tissue spaces as expressed in fig. 3, and this is obviously not the case. Thus after a careful study and interpretation of the silver reaction on the lymphatic vessels, on the albuminous fluid of the interspaces, and on the cell bodies of the connective tissue corpuscles, His was led to believe that the significance of the von Recklinghausen discovery was that lymphatics are lined throughout by an endothelium rather than that the silver method demonstrates open lymphatics.

III. EMBRYOLOGY.

1. Introduction.

It is, I think, clear that the problem in this state could only be attacked successfully by embryology with the purpose of establishing the fundamental morphology of the system. The importance of this is best expressed by His (44, p. 223), "Von den mancherlei offenen Fragen, die seit mehr denn 200 Jahren in den anatomischen Schriften

ueber das Lymphsystem discutirt zu werden pflegen, bietet wohl keine ein so unmittelbares physiologisches Interesse dar, als gerade die Frage nach dem Ursprung der Lymphgefässe in den Körperorganen. Mag man sich ueber die Bildung der Lymphe und ueber die bei ihrer Fortbewegung wirksamen Kräfte eine Theorie machen, welche man will, so fordert diese als ganz unerlässliche Grundlage eine praezisere Vorstellung von dem anatomischen Verhalten der ersten Wurzeln des Systems, sei nun eine solche Vorstellung wirklich aus der Beobachtung entsprossen, sei sie nur hypothetisch angenommen." It is without question that a comprehension of the relations of the lymphatic capillaries depends on an understanding of the fundamental morphology of the system.

2. Lymphatics as Dilated Tissue Spaces.

The relation of the lymphatics to tissue spaces formulated by von Recklinghausen was entirely in agreement with the early crude investigations of fœtal conditions recorded by Breschet (16). It was the practically universally accepted idea up to 1900 that lymphatics arose by the dilatation of tissue spaces caused by the fluid that exuded from the blood vessels; that this dilatation of the spaces began in the periphery, and that the vessels gradually approached the veins and joined them. Thus the growth of the lymphatic vessels was thought to be from the periphery to the center. This view was well stated in 1894 by Gulland (39), who found the lymphatics first in the subcutaneous tissue and then along the extremities in fœtuses, human, bovine and rabbit, between 3 and 4 cm. long, and thought that these vessels subsequently joined the veins. He thought that the force of the fluid in the tissues formed the lymphatics, so that they arose by an entirely different method from his conception of the origin of blood vessels (p. 467).

3. Budge's Work.

An account of the newer work on the origin of the lymphatic system must begin with Budge (17-22). Budge was led to a study of the lymphatic system in birds through noticing the great variations of the posterior lymph hearts in the adult (21). The posterior lymph hearts had been seen in birds by Panizza (103), A. F. J. Mayer (quoted by Stannius) and Stannius (142). Budge had already begun to study lymphatics in the adult liver (17) and in bone (18) by means of injection, and in 1880 (19) he described studies of a system of canals which he could inject in mesoderm of three-day chick embryos. These injections, which can be easily repeated, giving the exact patterns of Budge, were really made into the extraembryonic coelom, as has been shown by Mall (81) and myself (129), and have nothing to do with the lymphatics. They are not, as Budge himself noted, lined by endothelium; indeed Budge himself was most cautious in his interpretation, for he says (19, p. 325), "Mit Absicht habe ich den Ausdruck Lymphgefässystem für das eben beschriebene Canalsystem vermieden, weil mir hierfür noch nicht Anhaltspunkte genug gewonnen zu sein scheinen. Und doch liegt der Gedanke hieran nahe." In 1881 Budge (20) announced the important discovery that there was a plexus of lymphatic vessels accompanying the allantoic arteries of chicks easily injected from the sixteenth to the eighteenth day of incubation, and that these injections ran to the thoracic duct. The next year (21) in a fuller paper he described that these allantoic lymphatics not only entered the thoracic duct but drained into the posterior lymph heart, which played a great rôle in relation to the allantois. He injected the lymph heart through the allantoic vessels by the tenth day, and noted that the posterior lymph heart was preceded, as seen in the living chick (8 to 12 days), by veins, and that subsequently the lymph heart appeared, which could be distinguished by the fact that it pulsated with a different rhythm from the blood vessels. After Budge's death his work was brought together by His (22) and formulated somewhat in this manner: There are two lymphatic systems, a transitory and a permanent system, the first consisting of spaces in the extraembryonal membranes analogous to the coelom and found only in early stages. The second, consisting of the true endothelial-lined vessels which accompany blood vessels—which Budge so successfully injected. The thoracic duct he thought arose from the first system and was the only permanent part of the first system. Thus Budge's work, which was a reaching out into a dark field and had genuine important discoveries, was in line with the prevailing theory that lymphatics are related to tissue spaces, and introduced a misleading conception that lymphatics form after the same manner as the coelom and indeed in part as an extension of the cœlom as far as the primativ system and thoracic duct are concerned.

4. STATEMENT OF THE ARGUMENTS FOR THE VENOUS ORIGIN OF THE LYMPHATIC SYSTEM.

I shall now take up the proof of the theory that the lymphatic system is derived from the venous system, and will subsequently analyze the opposing theory, which, in its most recent from, is that lymphatics grow on the addition of tissue spaces (Kampmeier 66 and 66a).

The essential elements in the establishing of the venous origin of the lymphatics have been (1) the proof that lymphatic capillaries grow by the sprouting of their endothelial wall and not by the addition or hollowing out of connective tissue spaces. This argument is known as the method of growth by sprouting. (2) The proof that lymphatics gradually invade the body from center to periphery, establishing the point of lymphatic and non-lymphatic zones. This means that the main ducts grow as capillaries by the same method as the peripheral capillaries. This argument is known as the one of lymphatic and non-lymphatic zones. (3) That the original lymphatic ducts bud off directly from the veins. This is known as the origin of the lymph sacs by budding.

Thus the study involves three elements: The nature of the lymphatic capillary, the nature of the lymphatic ducts, and the nature of the first lymphatics or the lymph sacs. Each one of these three lines of proof involves the study of endothelium; the first lymphatics are buds from the endothelial lining of the veins; these endothelial buds invade the body down to the ultimate capillaries by the cell division of their endothelial wall.

A. GROWTH OF LYMPHATIC CAPILLARIES BY SPROUTING.

A study of the method of growth of lymphatic capillaries is necessarily associated with the study of the method of growth of blood capillaries, for as far back as the time of Schwann (139), who first saw the capillaries in the living tadpole's tail and who vaguely distinguished those which carried blood from those which had no corpuscles, there is a clear recognition that the two forms of capillaries grow by the same method. This method Schwann thought to be by the addition of hollow connective tissue cells.

The term growth by sprouting was introduced quite recently by His, but the first description of the process dates back to the year 1844, to the work of Platner (106) and of Prévost and Lebert (108). Platner described the growth of capillaries as seen in the living tadpole's tail. He analyzes Schwann's idea of the addition of cells as necessarily merely an inference from the appearance of the vessels in one stage, for when actually seen growing new cells are never added on. He says that rather each new vessel is a process of a preceding one and describes these processes as long, thin *Ausläufer,* which form loops and soon show a double contour. He says that the tiny processes never contain nuclei and are not cells, so that the interpretation of Schwann of the addition of cells could not possibly hold. Platner says that the same process of growth in the living tadpole had been observed by Prévost and Lebert. Indeed, in the same year (108) they published a series of four papers, in which they describe the growth of capillaries, not only in Batrachians, but more in detail in connection with the blood islands in the chick. They definitely use the term centrifugal growth and describe the process in the following graphic terms (p. 239): "Les vaisseaux poussent des saillies latérales par décollement partiel des lamelles du feuillet vasculaire, saillies plus ou moins arrondies ou pointues, allongées, formant des espèces d'éperons qui souvent finissent par se rencontrer, provenant de deux côtés différents, et établissent ainsi des vaisseaux de communication." They thought that the processes or "spurs" were for the most part hollow from the start and state that the larger vessels grew by the same method as the smaller.

In 1846 Koelliker published two papers (67 and 68), in one of which he announced the discovery of lymphatic capillaries in the tadpole's tail (67). He described the characteristic differences as seen in the living form between the two types of capillaries, the irregularities and more numerous processes of the lymphatics as well as their connection with the superior and inferior caudal lymph trunks. In the other paper he gives a most valuable analysis of the views of the early embryologists, Wolff, von Baer, Reichert and others on the problem of the growth of vessels. He takes up the various views of growth from spaces produced by fluids in the tissues as well as (5) by the (p. 118) which were then being discussed, namely, growth (1) by the addition of unbranched cells, or (2) by branched or stellate cells, or (3) by spaces hollowed out by the force of the heart beat, or (4) then new work of Platner, Prévost and Lebert, showing centrifugal growth, and concludes that the vascular and lymphatic capillaries grow by the addition of branched or star-shaped cells.

Four years later, 1850, Remak (125) rediscovered the lymphatics in the tadpole's tail by watching the living embryo, and, without knowing of the preceding work, he hurriedly published an even more graphic description of the form and growth of lymphatics than Koelliker's. Subsequently, after seeing Koelliker's work, he added a note (p. 182-183) to emphasize the fact that if the growth be watched in the living form star-shaped cells are never added—neither to the blood capillaries, nor to the lymphatic capillaries, nor, he adds, to the growing nerves. Many years later, 1886, Koelliker (71, p. 34), in an article mainly on nerves, corrected his view of the growth of the lymphatics by the addition of connective cells in favor of the theory of growth by sprouting.

The years from 1863 to 1867 represent a great advance in our conceptions of the lymphatic system. The historical article of His (44) on the lymphatic system must form the basis of any work which deals with the development of the problem. In 1865 Stricker (143) published a paper in which he expresses a doubt in regard to Koelliker's discovery of lymphatics in the tadpole's tail, on account of the fact that undoubted blood capillaries had also the blind sprouts. He, however, submitted the blood capillaries to an experimental study of great interest. He stimulated them with the vapor of ammonia and gives the following description of his results:

> Ich sah ein Gefässstück, welches seinem Baue nach unzweifelhaft zu den Kapillaren gezählt werden musste, sich im Laufe von fünfzehn Minuten zweimal bis nahe zum Verschwinden des Lumens verengern und bis zum Breitendurchmesser eines Blutkörperchens wieder erweitern. Ich sah varicöse Gefässe sich so veränderen, dass der Bauch an Stelle des Halses zu liegen kam, und umgekehrt. Mit den Formveränderungen ging gewöhnlich noch eine andere Veränderung Hand in Hand. So wurde beispielweise eine eingeschnürte Kapillargefässstrecke so blass, wurden deren Conturen so undeutlich, dass ich sie kaum mehr von der Umgebung unterscheiden konnte, während nach bis zwanzig Minuten das Gefäss wieder in seiner ursprünglichen Deutlichkeit zu sehen war.

Thus he discovered the contractility of endothelium. He found that electricity was a still better stimulant for observing this contractility. He discusses his results from the standpoint of determining the nature of the capillary wall, especially in connection with the silver preparations of Aeby, Auerbach and Eberth (quoted from Stricker 143), which has already given the suggestion of a lining of flattened cells for blood capillaries. Stricker saw clearly that the wall of the capillary was of living protoplasm, but was confused in regard to whether the blood stream was inter- or intra-cellular. He was perplexed also in regard to the existence of cells or not, since he was dealing with the growing tip, which we now know to be a syncytium. This idea occurred to Stricker, as is plain in these words, "Dass bei dem Aufbau von Kapillargefässen ueberhaupt Zellen mit einander verschmelzen, und dass solche Verschmelzungsspuren später einmal durch Silberniederschläge kenntlich werden können, lässt sich ferner auch nicht leugnen." Stricker also noted the sprouts of blood vessels as indicating their method of growth.

I have already taken up the fact that von Recklinghausen's work on the endothelium of lymphatic vessels, studied by means of the silver nitrate method, settled the question of the cellular nature of the lining of lymphatics, especially in connection with the analysis of the work by His, who had regarded lymphatics as vessels without walls (44, p. 229), and saw by a thorough study of preparations made by the silver method that lymphatics were lined throughout by endothelium.

In 1867 Langer (75), as a conclusion to a series of studies on the lymphatic system in amphibia, published a study of the lymphatics in the tadpole's tail. He was able to make complete injections of the blood vessels and the lymphatics and gives a most interesting analysis of specimens as observed in alcohol from the standpoint of weighing the evidence on the method of growth. He describes the uninjected capillary as often appearing to have a single contour, while the injected one had the complete wall. He could not find in the alcoholic specimen the tiny processes previously described in the living form. He noted, however, the larger sprouts, the loops and blind processes, and says that the nuclei are definitely within the contour of the wall of the capillary, so that he makes the distinction between the vessel and the surrounding tissue. He concludes that the various forms of the processes must indicate the process of centrifugal growth for the lymphatic capillary as well as for the blood capillary.

Again in 1873 the growth of the lymphatics and blood vessels by the method of sprouting was observed in the tadpole's tail and very clearly described by Rouget. By the use of curare he was able to keep the larva still. He also emphasizes the great number of tiny filaments on the lymphatics and the fact that they never join with the connective tissue cells.

Thus the observation of the growth of capillaries by sprouting was made over and over again where there was the chance of seeing the process in the living form or of obtaining injected specimens, and yet during all these years the observations were not generally accepted, since as the fundamental morphology of the lymphatic system was unknown, the significance of the observations could not be understood.

It is, however, not true that every observer who studied the living tadpole's tail described the process of the sprouting of the endothelial wall of blood vessels and of lymphatics as showing the method of growth. Indeed at least three observers have doubted whether there are two different kinds of capillaries in the tadpole's tail. I have already noted that Stricker doubted the presence of lymphatic capillaries in the tadpole's tail.

Wysotzky (155), whose work, since it is published in Russian, I quote from Mayer (89), thought that the capillaries without blood were merely young blood capillaries.

Sigmund Mayer (89), in an interesting and valuable paper, "Ueber die Blutleerengefässe im Schwanze der Batrachierlarven," gives first an excellent analysis of the literature on the subject of the capillaries in the tadpole's tail. He brings out the fact that it was the presence of an occasional red corpuscle in the "lymphatic" which was the stumbling block in accepting the presence of lymphatic capillaries. He then records an observation which in reality cleared up the entire difficulty in regard to the "empty capillaries." As E. R. Clark (26) has shown, Mayer, however, failed to see the bearing of his own observations. Mayer used curare and the electric current to anæsthetize the larva and then covered the tail with a cover slip. When he sucked the water out from under the cover slip he noted that the blood would gradually stop flowing or even go in the reverse direction in the blood capillaries and that the vessel would collapse, so that it looked like a solid cord. Thus he also observed the contraction of endothelium. Furthermore, he noted that the "other empty vessels" (namely, lymphatics), contracted more frequently than the blood capillaries. When, however, he studied these other empty vessels he thought that the occasional cells in them flowed now toward the center, now toward the periphery, and he ended with the somewhat vague and erroneous conclusion that the empty vessels, though they might have some of the functions of the lymphatics of the adult, could not properly be grouped with them. We now know that the two sorts of empty vessels are (1) the collapsed blood vessels which Mayer himself observed and (2) the true lymphatics (E. R. Clark, 26).

The work of Mayer, however, has another point of great interest to us beside the important observation of the contractility of endothelium, namely, what we call Mayer-Lewis anlagen. Mayer noted the long strands of cells (endothelium) which often span the gap between two capillaries; indeed, he figures them, some that look entirely solid and some that have, here and there, a patent lumen. In reality both blood capillaries and lypmhatic capillaries have these strands and sprouts, and it is one of the most remarkable qualities of the two forms of endothelium that no sprout from a lymphatic capillary ever joins a blood capillary and vice versa. However, Mayer's mistaken idea that these strands of cells connected with two different kinds of capillaries, namely, the vessels which are always empty, in other words, the lymphatics and the blood capillaries, aided in his confusion of the lymphatics with the blood vessels. Besides these strands of endothelium he saw small hollow vessels, having the same lining as the capillaries, which he thought to be entirely isolated. These he interpreted as follows (p. 236):

> Unseren Erfahrungen nach sind nun die beschriebenen Bilder nur gewisse Stadien der Ausschaltung von Bestandtheilen des Blutgefässystems aus der normalen Circulation. . . . . Bei genauerem Studium der letzteren Formationen ergibt sich, dass die Wandungen derartiger mit freien Spitzen in das Gewebe hineinragenden, und ausserhalb jeder Kommunication mit Gefässröhren stehenden Fragmente bezüglich des Aufbaues ihrer Wand entweder mehr den Typus der blutleeren oder demjenigen der bluthaltigen Röhrchen sich nähern.

Most of the apparently isolated anlagen seen in sections are due to the collapsing of the vessels which connect them with the rest of the capillaries through the contractility of the endothelium which Stricker and Mayer observed. In sections they may occur in great numbers through the contraction of the endothelium due to the fixing agent. The possibility of entirely isolated vessels and the meaning of the apparently isolated vessels are fully discussed later in connection with the theory of the growth of lymphatic capillaries by the addition of Mayer-Lewis anlagen in section VIII.

If it be established that the peripheral capillaries grow entirely from preceding capillaries, then it is a perfectly logical hypothesis that the lymphatics grow from the veins, from center to periphery, rather than from the periphery to the veins. This hypothesis was advanced by Ranvier (113), based on the evidence of the method of growth of the lymphatic capillaries within the peripheral plexus. Ranvier (110-118), in a series of studies between the years 1895 and 1897, made injections of lymphatics in a variety of embryos. For example, he injected the exceedingly abundant plexus in the mesentery of a fœtal pig 10 cm. long, as well as in the rat and rabbit. He also injected the lymphatics in the amphibia. These injections gave him an extensive knowledge of the form of the developing lymphatic plexuses, the valves looking like collarettes in the walls of lymphatic ducts, the irregular capillaries with blunt terminal knobs, of which especially large ones are often found in the mesentery as well as the slender sprouts, either ending free or as bridging a gap in the network to another vessel. From all of these forms of growing lymphatics Ranvier saw that the growth of lymphatics was from center to periphery, and even though he thought that the lymphatics did not begin in a mammalian embryo until it was about 10 cm. long, a stage at which the embryology of the system may be called complete, nevertheless he went a step farther than all of the preceding observers, for he deduced the hypothesis that the lymphatics grow from the veins. He likened their growth to the growth of a gland (113). In my own work I was led to the same view by tracing the lymphatics in younger and younger embryos back to the veins, and the next section will include the evidence which I regard as essential to establish the hypothesis of Ranvier as the correct theory of the origin of the lymphatic system. The account of the evidence for growth by sprouting is, however, not yet complete. As far as the evidence can be obtained by the observation of injected specimens, it was especially well described and figured by MacCallum (79). He added the observation of watching the injection under the microscope and showed that extravasations are due to explosive rupture of the lymphatic wall.

Injected specimens of developing lymphatic capillaries are now well known; excellent figures are given by Bartels (10, figs. 9 and 10, p. 43). They show a large number of sprouts, because they are taken from the skin of a pig embryo 6.5 cm. long. This is the exact stage when the secondary, superficial, fine-meshed plexus is just growing from the deeper coarse-meshed or subcutaneous plexus, and, since the secondary plexus is growing actively, it shows many sprouts.

The proof of growth by sprouting from injections is always an interpretation of appearances, and though it is a logical inference, one must turn to the observations of the living form for conclusive proof. This has been given by E. R. Clark (25-26), who has again restudied the classical object, the tadpole's tail. The introduction of chloreton anæsthesia is one of the factors that have made this study possible, since the same specimen can be kept alive for weeks, notwithstanding repeated doses. Dr. Clark's devise of an upright chamber, so arranged that the tadpole can be kept upright without the pressure of the cover slip, and the finding of larva of the form Hyla pickeringii in the spring of 1910, a form which has few pigment cells, have all combined to make his studies so valuable and convincing. He has described not only the complete history of a lymphatic capillary, watched through periods of weeks, but has followed every connective tissue cell in the neighborhood (30) through several generations. Dr. Clark has shown that the wall of the lymphatic capillary is in ceaseless activity. In the living form the wall is in part hyaline, in part granular. The nuclei are surrounded and obscured by granular protoplasm, so that they are clearly seen only when dividing. The wall is of irregular thickness, often extremely delicate, and from the sides and tips are sent out numerous tiny processes, some hyaline and some granular, which may be well described as amœboid. A few of these persist and grow into permanent lymphatics. Most of them are withdrawn. These tiny sprouts, indicating the functional activity of the vessel, do not disappear in alcoholic specimens (26, p. 403). They are at first without nuclei, but nuclei wander into them from the parent stem; indeed, two nuclei may pass each other as they advance or recede. This proves that the growing amœboid wall of the lymphatic capillary is a syncytium and explains the failure to obtain the silver markings at the growing tip. The silver markings indicate the more stable lymphatic capillary.

E. R. Clark's most recent observations (30) show that increased activity of the lymphatic wall in the sending out of many of the tiny processes is a sign of growth, so that an area can thus be selected to watch the processes of the formation of new vessels.

As far as the relation to the surrounding connective cells is concerned, the growing, and, we might also say, the functioning, amœboid tips avoid the cell bodies and processes of the mesenchyme cells.

Thus there can be no question in regard to the method of growth of the peripheral capillaries. Both blood and lymphatic capillaries grow by the activity of the protoplasm of their walls. The endothelium at the growing tip is a syncytium, the processes advance and recede; they are tiny, hair-like vessels, and they receive their nuclei from the parent stem. There are differences in the appearance of the two types of capillaries probably associated with the presence and absence of the circulating blood and the difference of function. The lymphatics have very many more tiny sprouts, only a few of which are permanent; that is, their wall is much more amœboid and the vessels much more irregular. Thus on positive evidence, namely, the observation of the process in the living form, which is the best evidence known to anatomical science, we are justified in the conclusion that capillaries grow by sprouting.

B. LYMPHATIC AND NON-LYMPHATIC ZONES.

The second argument in favor of the venous origin and the centrifugal growth of lymphatics by their own endothelium is that it can be shown that lymphatic vessels gradually invade the body from certain limited centers. Thus if injections of vessels are made from these centers in larger and larger embryos an ever-increasing zone of lymphatic capillaries can be demonstrated. Moreover, for each stage the zone of vessels is constant.

I began my work with the study of the development of lymphatic glands in the embryo pig and to obtain injections of them introduced the needle into the foot pads. By taking younger embryos a stage was soon reached when no injections of the foot pads ever entered lymphatics, but at these stages one could still inject lymphatics in the skin over the body. This was the beginning of the proof that lymphatics bud off from the veins and grow peripheralward instead of the reverse (Sabin 129).

In an embryo pig 5 cm. long (Sabin 130, fig. 5) a simple plexus of lymphatic capillaries has almost entirely covered the body. I say capillaries advisedly, adopting Ranvier's (118, p. 74) criterion of valves for lymphatic ducts in contrast to their absence in the capillaries. The body is first invaded by lymphatic capillaries, and the primary plexus shown in fig. 5 (Sabin 130), which is the anlage of the deep, subcutaneous plexus, was injected by a single puncture of the needle.

Subsequently this plexus develops valves, but at this stage the entire lymphatic system can theoretically be injected from any one vessel, because there are no valves, or, in other words, because it is entirely a capillary system. Nearly the same stage is shown for a human embryo in figs. 505 and 506 (Sabin 134). This was a remarkable specimen, in which air filled the lymphatics, and it has the additional interest of showing the beginning of valves in the vessels of the skin, namely, those of an occipital duct and in the axillary and inguinal ducts.

If earlier stages of embryo pigs are taken the cutaneous vessels, as shown by injecting them, gradually recede, as seen in figs. 1 to 4 (Sabin 130), to two points, one in the neck and one in the groin. The earliest lymphatics reach the skin in the neck of an embryo pig about 18 mm. long. All injections of the lymphatics of the skin of the anterior part of the body between the stages of 2 and 5 cm. long can be seen to run into two symmetrical sacs in the neck close to the jugular vein. These anterior lymph sacs, which have now been identified in a very great number of forms, can be found in pig embryos in earlier stages than the first cutaneous lymphatics. In my first paper I traced them back to the stage of 14 mm., when they are small empty sacs, close against the anterior cardinal vein. In reality they begin in the pig of 10 to 11 mm. and their method of origin will be discussed in the next section.

The argument of lymphatic and non-lymphatic zones thus consists in the fact that the first lymphatics are sacs close to the veins, and from this stage onward lymphatics can be injected in wider and wider zones until they cover the entire surface of the body.

It is necessary to prove that each zone represents the limit of the growth of the lymphatics for a given stage. To prove an injection is complete for any stage such as one shown in fig. 6 (Sabin 135), it is essential to have abundant material and to show by injection that the lymphatic tips always rupture along a given line when the pressure is increased. The shape of the lymphatic vessels at the line of growth will vary according as the vessels are progressing rapidly or not; for example, the rounded ends of fig. 2 (Sabin 129) are from an area where lymphatics grow slowly, while the margins of fig. 6 (Sabin 135), with numerous pointed sprouts, are from a rapidly growing zone. Furthermore, sections of the skin in the lymphatic and non-lymphatic zones show a sharp contrast in the presence or absence of the large lymphatic capillaries, fig. 6 (Sabin 130), which are easy to identify. The method of sections is, however, inadequate to define the limits of growth, except for the large vessels, for the tiny lymphatic sprouts can only be found in sections when the plane of cutting is favorable.

This progression of the lymphatics in the skin has been confirmed by Polinski (107) in bovine embryos. The patterns which he shows make a most interesting comparison with those of pig, cat and human embryos. In the bird the same progression of zones is shown to some extent in the injections of Mierzejewski (96).

Beside the definite zones the lymphatics grow into definite layers. Ranvier (118) noted that the superficial lymphatics are deeper than the blood vessels. They follow the vessels into the skin and each plexus is deeper than the corresponding blood vascular plexus (Sabin 130). The development of the lymphatics into the intestine, as worked out by Heuer (43), illustrates the point of the definite layers into which the lymphatics grow particularly well. The lymphatics for the intestine grow from the retroperitoneal sac, which arises from the renal veins (Baetjer, 8). The vessels form a rich plexus in the mesentery and from this plexus a series of vessels grow into the intestinal wall and penetrate to the submucosa. Here they form at first a series of units shown by Heuer in fig. 10 (43), which has been copied as fig. 508 (Sabin 134). These primary vessels soon form the submucosal plexus of ducts, from which the mucosal capillary plexus and lacteals develop on the one hand and the serosal vessels on the other.

This fact, that the body is invaded by lymphatics, has an especial interest, because it was the clue which enabled us to trace back the systems of lymphatic ducts to their beginnings and show that they arise from the veins and grow toward the periphery. It is, furthermore, the key by which the development of the lymphatic system within each organ may be traced to the ultimate capillaries. It is considered again in relation to the development of lymph sacs, for there it can be taken up in connection with its exact relations to vascular and non-vascular zones. Both the blood vascular and the lymphatic systems invade the body by the growth of their capillaries. Each system has its definite zones and layers which can be followed in orderly progression. The invasion of the body by the blood capillaries is more complete than by the lymphatic capillaries; for example, the lymphatic capillaries do not grow into the central nervous system, nor into the interspaces between muscle fibers.

C. DIRECT BUDDING OF THE LYMPHATICS FROM THE VEINS.

As has been stated, it was the study of the decreasing zones of lymphatic capillaries which led to the discovery that the first lymphatics are sacs close to the veins. In mammalian forms the first lymphatics are the anterior lymph sacs which bud off from the anterior cardinal veins. These jugular lymph sacs were noted by Saxer (138) in 1896 in his extensive study on lymph glands, but he did not recognize their significance. They can readily be made out in sections of pig embryos 14-20 mm. long, or in sections of any mammalian embryo of the corresponding stages. The fact that they are the first lymphatics in mammals and that they lie close to the vein, separated only by the double endothelial wall, led me to the conclusion that the lymphatics budded directly off from the veins and it is gratifying to find that this reasoning has been justified by further investigation (Sabin 129, E. R. & E. L. Clark 29 and Hoyer 49a).

To follow the development of our knowledge in historical sequence the next step was taken by F. T. Lewis (76) in a series of excellent reconstructions of the anterior lymph sacs in rabbit embryos, the best figures we have had up to the present time of the form of the early sac. Lewis carried the study still further back and showed that the definite sac was preceded by a blood-filled capillary plexus. This blood-filled plexus has proved to be a very important observation. From the presence of blood Lewis made the logical inference, with the evidence at his command, that these vessels were blood capillaries and that hence lymphatics were transformed blood capillaries. The observation of the blood-filled vessels has been confirmed by Huntington and McClure (54) on the cat and by myself in human and pig embryos (132-133) and we have all accepted the theory of transformed capillaries until new evidence has now shown us the correct explanation of the presence of the blood.

This new evidence has been furnished by the work of E. R. and E. L. Clark (27-29). E. L. Clark began with the study of the allantoic lymphatic vessels in chick embryos. From the allantoic vessels she was led back to the posterior lymph hearts and the lymphatics of the body wall. The injections of Mierzejewski (96) show that the primary line of growth for the lymphatic vessels in the skin of the chick is along the thoraco-epigastric vein (96, figs. 1 to 4). E. L. Clark noted that in early stages the lymphatic vessels along this line were filled with blood and that the blood in them was stagnant, in striking contrast to the rapidly circulating venous blood. The fact that the lymphatics invade the skin in the chick while they are in the blood-filled stage gives at once an advantage. By means of fine glass cannulas E. L. Clark was able to inject individual vessels of this blood-filled plexus in the living chick and watch the ink flow to the pulsating lymph heart and thence to the veins. These blood-filled vessels have the usual characteristics of lymphatic capillaries, in that they are larger and more irregular than blood capillaries, but the essential point in E. L. Clark's work is that by using a form in which the lymphatics could be seen in the living embryos she discovered a new criterion for recognizing lymphatics, namely, the stagnant blood in contrast to the circulating blood.

With this important criterion she has followed back the origin of the posterior lymph hearts. Since Sala (137) it has been known that in the chick the posterior lymph hearts develop opposite the lateral branches of the first five coccygeal veins (137, p. 269). Sala described the process as beginning during the sixth day by a hollowing out of spaces in the mesenchyme, but by watching the living chick embryo during the fifth day E. R. and E. L. Clark have seen that the skin over the first five coccygeal veins is a comparatively non-vascular zone, so that brilliant direct illumination enables them to see in the depth a series of tiny blood-filled buds close to the main coccygeal vein and its branches. The blood in these buds is of slightly different color from the circulating blood. They proved that these buds are always in connection with the parent vein, for a direct injection of them always runs over into the vein, but no injection of the peripheral blood capillaries ever fills them. Hence they bud off from the veins and are filled with blood from a back-flow from the parent vein. It is of course evident that this process cannot be seen in the body wall of the chick with the clearness with which every cell division can be followed in the tadpole's tail; nevertheless, the stagnant blood has been proved by injection to practically fill the developing vessels, so that it is an adequate criterion of the extent of their development.

By selecting a chick which shows these primary lymphatic buds and keeping it under observation under high power in a warm chamber E. R. and E. L. Clark (29) have been able to watch these blood-filled lymphatic buds join with each other to form a deep circumscribed lymphatic plexus, the anlage of the posterior lymph heart. It is clear from Sala's description that it was this plexus which he described as the beginning of the lymphatics. While the deep lymphatic capillary plexus is being transformed into a lymph sac and pulsating lymph heart, lymphatic vessels are already growing toward the skin, where they gradually extend. They grow first along the lateral line to anastomose with the jugular lymphatics. There is a continuous peripheral growth of the lymphatics from the time of the first buds on, and the entire blood-filled stage takes but a few hours. Nevertheless, it is long enough to enable one to watch the buds form a plexus; the plexus becomes a sac and lymph heart, and the lymphatics from it spread out in the skin. Injections prove that in every stage of their development, from the primary buds onward, the lymphatics connect with the parent veins; thus there is no separation from the vein and subsequent rejoining, as all of the recent workers, Lewis, Huntington and McClure and myself, have thought from the difficulty of finding the connections with the veins in serial sections.

The posterior lymph heart in the chick is especially advantageous for study, since it is in the first place sufficiently superficial to be seen in the living embryo, and in the second place it is covered by a non-vascular zone. In mammalian embryos no caudal lymph hearts develop. It is very interesting to note in injected embryo pigs that the corresponding area in the skin at the root of the tail, instead of being a non-vascular zone, is an area of especially wide blood capillaries. This area, seen in fig. 467 (Evans 35), is constant, and, as it almost always retains a little blood, can be injected when a partial injection of the veins of the lower part of the body is desired.

The work of the Clarks adds the final proof of the theory that the lymphatics bud off from the veins. Moreover their method is so simple that anyone may convince himself of the essential results by a few hours observations. Their injections have corrected two errors, namely, the idea that the lymphatics are transformed blood capillaries and that they temporarily separate from the veins.

Thus I regard as proved the three points which have been stated as essential in establishing the origin of the lymphatics from the veins. Stated in reverse order they are: First, the lymphatic system begins as a series of endothelial buds which sprout out directly from the veins as a new type of vessels, namely, lymphatics. These buds unite to form plexuses which develop into sacs. These sacs may become lymph hearts. Second, from these lymph sacs or hearts lymphatic capillaries gradually invade the body in orderly sequence in definite and characteristic zones and layers. The growth is always in the capillary bed, that is, all lymphatics develop as capillaries, and the earliest ones to develop become the first lymph trunks or ducts. Third, the method of growth throughout is by the sprouting of the protoplasm and the nuclear division of the endothelial of the capillary wall. The ultimate capillaries are distinguished by the absence of valves. In a word, there is a continuous growth and invasion of the body by lymphatic capillaries from the primary sprouts which bud off from the veins to the ultimate peripheral lymphatic capillaries.

IV. PRIMARY LYMPHATIC SYSTEM IN DIFFERENT FORMS.

1. Primary Lymphatic Sacs in the Pig.

A. GENERAL SUMMARY OF THE SACS.

I shall begin the section on the special anatomy of the lymph sacs by a detailed description of the origin of the lymphatics in the pig, since that is the best known form. I can now describe the origin of all of the lymphatic sacs in the pig and give the relation of the main ducts to all of these primitive sacs. On the basis of our knowledge of the lymphatic system in this form I shall give what is known of the lymphatic system in other mammals, in birds, reptiles and amphibia, and shall then be in a position to compare the primary lymph sacs in mammals with the amphibian lymph hearts and sacs.

In the pig the lymphatics bud off from the veins in two places, from the anterior cardinal veins and from the veins of the Wolffian body. There are two sets of paired sacs, the jugular and the iliac; and two unpaired sacs, the retroperitoneal and the cisterna chyli. In the most general terms the jugular sacs drain the anterior half of the body; the iliac sacs drain the posterior half of the body, while the retroperitoneal or præ-aortic sac drains the viscera. The cisterna chyli with the thoracic duct connects the jugular and renal lymphatics. In more specific terms the jugular lymphatics bud off from the anterior cardinal veins, form large sacs in the neck, from which lymphatics grow to the head and neck, the foreleg and thorax, and to the heart and lungs. From the left sac arises the jugular stem of the thoracic duct. All the rest of the lymphatic sacs bud off from the vena cava, where it is a part of the median mesonephritic vein, from the median mesonephritic vein and the veins in the dorso-medial edge of the Wolffian bodies. The lymphatics which grow from the ventral surface of the mesonephritic veins make the large retroperitoneal or præ-aortic sac; those which grow along the dorso-medial edge of the Wolffian bodies, lateral to the aorta, form the iliac sacs, and those which grow dorsal to the aorta make the cisterna chyli and thoracic duct. The thoracic duct is formed in small part from a duct from the left jugular sac; in larger part from a plexus which surrounds the aorta from the cisterna chyli. The retroperitoneal sac drains the diaphragm and the abdominal viscera, except the permanent kidney; the iliac sacs drain the permanent kidney, the abdominal walls, the hindlegs, tail and embryonic membranes.

B. THE JUGULAR SACS.

As has already been stated in part III, the spreading of the primary superficial lymphatic capillaries in the skin of the embryo pig takes place while the embryo is growing from 20 to 50 mm. long. The first lymphatic buds are found when the embryo is about 11 mm. long (fig. 6); the sac is well formed at 18 mm. (fig. 7), and reaches its maximum size in an embryo 30 mm. long (fig. 8). It remains as a large sac until the embryo measures 50 mm., when it begins to be transformed in part into lymph glands (fig. 16).

An understanding of the development of the jugular sac depends on a knowledge of the veins of the region. Indeed, I was not able to inject the early stages until I had so mastered the pattern of the blood vessels that a little blood in any of them enabled me to reproduce the whole picture and so avoid the blood vessels.

The study of the form of the early anterior cardinal vein is shown for the chick by Evans (34) in his figs. 1 to 3. These figures show that the primitive deep dorsal segmental branches drain the ventrolateral surface of the spinal cord. They bring out the gradual curve of the anterior cardinal vein and the more marked bend of the posterior cardinal vein, where the two join the duct of Cuvier. This stage is shown for the chick in cross section by Evans (35) in his fig. 437 B, as well as in (Evans 34) his fig. 4.

In fig. 4 is given an injection of the blood vessels in an embryo pig 7 mm. long, a stage just before the lymphatics begin. The curve of the dorsal border of the cardinal veins toward the duct of Cuvier is slight, not as marked as in the chick, nor as it is on the left side of this same embryo.

Arising from the cardinal veins there is a series of seven deep segmental branches extending to the nervous system between the area of the primitive posterior cerebral vein (Mall 143), which arches downward over the medulla and cord and the cerebral end of the arm bud. The first two of these branches drain the medulla, and hence there are five spinal or segmental branches proper. Each of these branches has a corresponding artery which lies slightly caudalward and nearer the midline. Only the lower four segmental arteries are injected in this specimen. The relative position of artery and vein

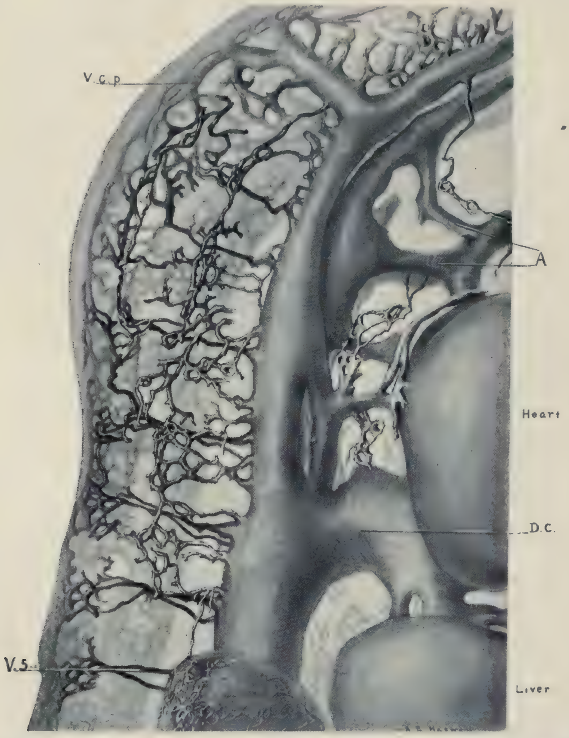

FIG 4.—Injected specimen to show the anterior cardinal vein and its branches in an embryo pig which measured 7 mm. in its greatest diameter. Magnified about 28 times. This is a stage before the lymphatic vessels have begun. A = aorta arches; D. C. = duct of Cuvier; V. c. p. = vena cerebralis posterior; V. 5 = fifth segmental vein.

shows in fig. 437 (Evans 35). Each of the five spinal veins drains a plexus of wide capillaries, which marks the presence of the developing spinal ganglia.

It is, however, the superficial veins which are of more interest from the standpoint of the lymphatic system. Along the dorso-lateral border of the cardinal veins there is a series of intersegmental sprouts, varying from one to four or five in each interspace. These sprouts drain a superficial capillary plexus which is developing in a groove in the neck which is a continuation of the groove dorsal to the Wolffian ridge. The arteries for this superficial capillary plexus come from the deep segmental arteries (Evans 35, fig. 437). The connections of the plexus with the cardinal vein are most abundant near the posterior cerebral vein. This superficial capillary plexus of the body wall has a most interesting development. For the area between the limb buds it has been worked out by Dr. Helen W. Smith (141), whose figures are copied by Evans (35). This superficial plexus in the tail region shows a constant zone of widened capillaries (35, fig. 467) corresponding to the position of the posterior lymph hearts in birds. For the neck region it is necessary to know this plexus in order to locate the jugular lymphatics, and therefore its development will be followed in further stages.

The ventral branches of the anterior cardinal vein are represented at this stage by one large pericardinal vein, which receives branches from the gill arch region. The common stem for the branchial and pericardial vessels connects with the anterior cardinal vein, but it drains directly into the duct of Cuvier (see Grosser and F. T. Lewis as quoted by Evans 35, p. 660) on the right side of this embryo, while on the left side of the same specimen it opens into the anterior cardinal vein.

The earliest lymphatic buds have been found in embryo pigs measuring from 10 to 11 mm. long. All of my measurements mean the greatest length and are made on the fresh specimen. The stage of the first lymphatics is shown in two figures, fig. 5, a total mount of an embryo injected with India ink through the umbilical artery in a specimen 11 mm. long, and fig. 6, a cross section 250 μ thick, through the lymphatic area in an embryo measuring 11 mm. The blood vessels were injected with India ink, and the lymphatics are filled with blood.

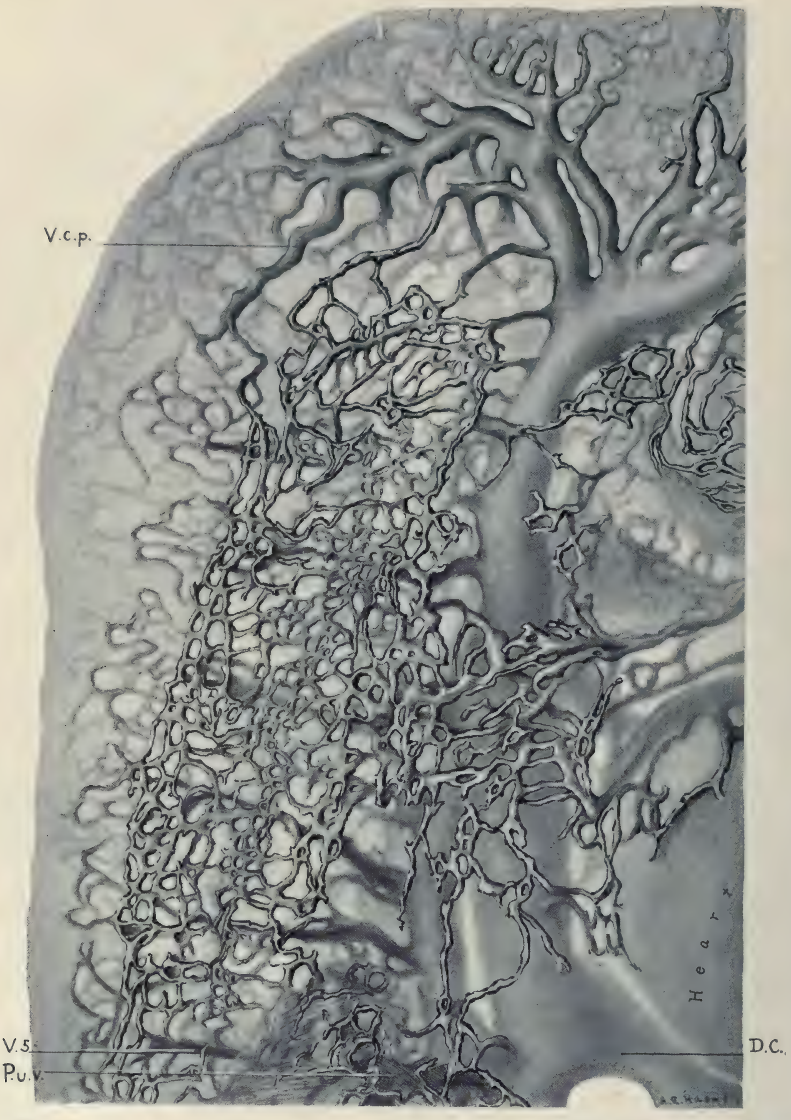

FIG. 5.—Injected specimen of the anterior cardinal vein and its branches in an embryo pig measuring 11. mm. in its greatest diameter. Magnified about 33 times. This is the stage at which the lymphatic vessels begin to develop. The vessels were injected with India ink through the umbilical artery. D. C. = duct of Cuvier; V. c. p. = vena cerebralis posterior; P. u. v. = primitive vena ulnaris; V. 5 = fifth segmental vein.

The blood vessels show a great development. The five spinal segmental veins are clear, draining the large plexuses around each spinal ganglion; the ganglia are now farther ventralward than in the preceding stage. The superficial capillary plexus shows the most marked changes. There is a continuous sheet of superficial capillaries in the neck, anastomosing with the branchial vessels, with the pericardial vessels and with the abundant capillary plexus of the arm bud. Opposite the medulla the connections of this superficial plexus with the anterior cardinal vein are very numerous, while opposite the heart a few veins connect it either directly with the anterior cardinal vein or more frequently with the main segmental branches. It is this

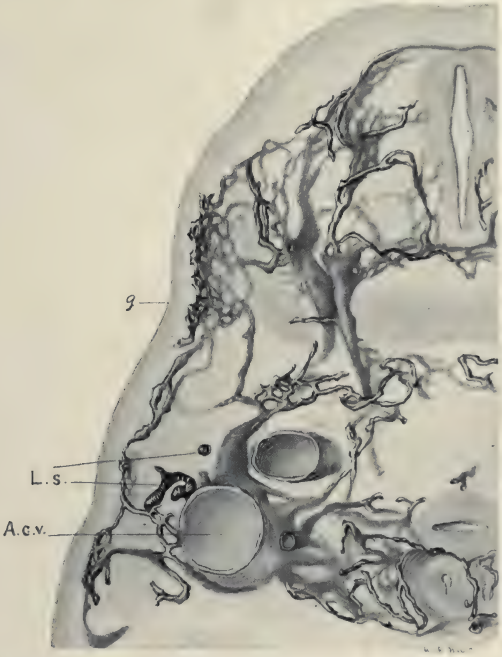

Fig. 6.—Section through the third segmental vein in an injected embryo pig which measured 11 mm. in its greatest diameter. The section, which is 250 μ thick, shows the relation of the jugular lymphatic sprouts or buds to an anterior cardinal vein. Magnified about 40 times. The blood vessels were injected with India ink through the umbilical artery. The lymphatic sprouts, L. s., have a natural injection of blood; these lymphatic sprouts lie in a non-blood-vascular zone dorso-lateral to the anterior cardinal vein. A. c. v. = vena cardinalis anterior; g = groove.

zone, opposite the third, fourth and fifth segmental veins, that is the lymphatic area.

To locate the lymphatic area definitely it is necessary to note the details of the superficial veins more carefully. The superficial plexus along the lateral groove is finer meshed and of smaller capillaries than the rest. The groove is an important land mark and it shows best in the cross section, fig. 6. From the plexus in the groove a sheet of wide capillaries is growing dorsalward external to the myotomes, and loops from this sheet connect with the deep plexus around the spinal cord. The skin over the entire dorsal surface of the cord is an entirely non-vascular area at this stage. From the ventral border of the superficial plexus in the groove a sheet of wider and more open-meshed capillaries covers the surface of the embryo over the anterior cardinal vein. The surface contour of this, the lymphatic area, is a swelling seen in fig. 6, which I shall call the jugular lymphatic ridge. The blood capillaries of this area are very superficial and drain into the cardinal vein in four ways: (1) Through the plexus in the groove and its dorso-lateral superficial veins; (2) in small part through direct branches to the lateral surface of the cardinal vein; (3) through branches of the ventro-lateral surface of the anterior cardinal vein which drain the pericardium (fig. 5); and (4) through anastomoses with the capillaries (fig. 5) of the primitive ulnar vein. The primitive ulnar vein has developed from the diffuse capillary arm bud plexus of the preceding stage. It enters the lateral surface of the posterior cardinal vein directly opposite the fifth segmental branch. Thus a part of the blood of the branchial region and of the pericardium drains through the superficial plexus over the lymphatic ridge into the primitive ulnar vein. In a little older embryos, namely, those 12 mm. long, a second vein has developed from the arm bud plexus just cerebralward to the primitive ulnar, which now receives the blood from the plexus of the lymphatic ridge. The complete description of this superficial plexus involves a study of the origin of the external jugular vein which I do not wish to go into until I can illustrate it adequately. I bring up the point here because A. H. Clark (24) has shown that occasionally a lymph trunk in the neck in older pigs opens directly into the external jugular vein near its point of union with the internal jugular vein. It is therefore of importance to note that the capillary plexus in the arm bud, from which this part of the internal jugular vein comes, is present in the embryo when the lymphatics are budding out, though the internal jugular vein as a whole is formed considerably later.

For the present the interest in the superficial blood capillary plexus is that it covers the lymphatic ridge. It will be seen in fig. 6 that the lymphatic ridge includes a non-vascular area. This non-vascular area is bounded by the anterior cardinal vein and its dorsal branches, the plexus of the groove, the wide-meshed superficial plexus and the ventro-lateral branches of the anterior cardinal vein. An occasional direct lateral branch of the cardinal vein cuts through the otherwise non-vascular area. Within this area are seen the blood-filled lymphatic buds. They lie in the angle between the anterior cardinal vein and its dorso-lateral branches and connect with both. They are opposite the third, fourth and fifth dorsal segmental veins, and extend a distance of 1.5 mm. from the primitive ulnar along the anterior cardinal vein. The tiny lymphatic buds are already sending sprouts away from the parent vein.

The presence of stagnant blood, which has proved so valuable a criterion in the living embryo, must be used guardedly in studying sections, unless there is a complete vascular injection. In the lymphatic area I have noted in the fresh embryo that the blood capillary plexus of the groove is often empty, while the superficial plexus over the lymphatic area and over the pericardium tend to retain some blood. The blood vessels of an area where lymphatics are budding must be thoroughly known before one can be sure of the lymphatic buds. The early lymphatic buds are packed with blood to an extent not common for the veins, which perhaps shows best in figs. 490 and 491 (Sabin 134), for the jugular lymphatic buds in a human embryo.

I have not yet succeeded in injecting the first jugular lymphatic buds in the pig as E. L. Clark has done for the early stages of the posterior lymph heart of the chick. In the embryo 12 mm. long they can be seen in the fresh embryo, and sections show that they have formed a plexus along the margin of the anterior cardinal vein. To see the lymphatic buds at 12 mm. the embryo should be placed in warm Locke's solution while the heart is still beating, and it should be viewed under the high powers of the binocular microscope with the direct sunlight focused upon it. The lymphatic area is wider in the dorso-ventral direction than in fig. 6, but its dorsal boundary is clearly marked by the surface groove. If the superficial blood capillary plexus is empty the lymphatics can then be seen looking like a cluster of dull red grapes against the cardinal vein; in the older specimens some of the buds are markedly larger than others, while at 14 mm. the largest of them makes a definite sac with large sprouts projecting dorsalward. At this stage, namely, 14 mm., the sac can be injected by direct puncture. The preceding or plexus stage is shown by E. L. Clark for the corresponding sac in the chick in fig. 15. The beginning sac is shown for the human embryo in fig. 491 (Sabin 134).

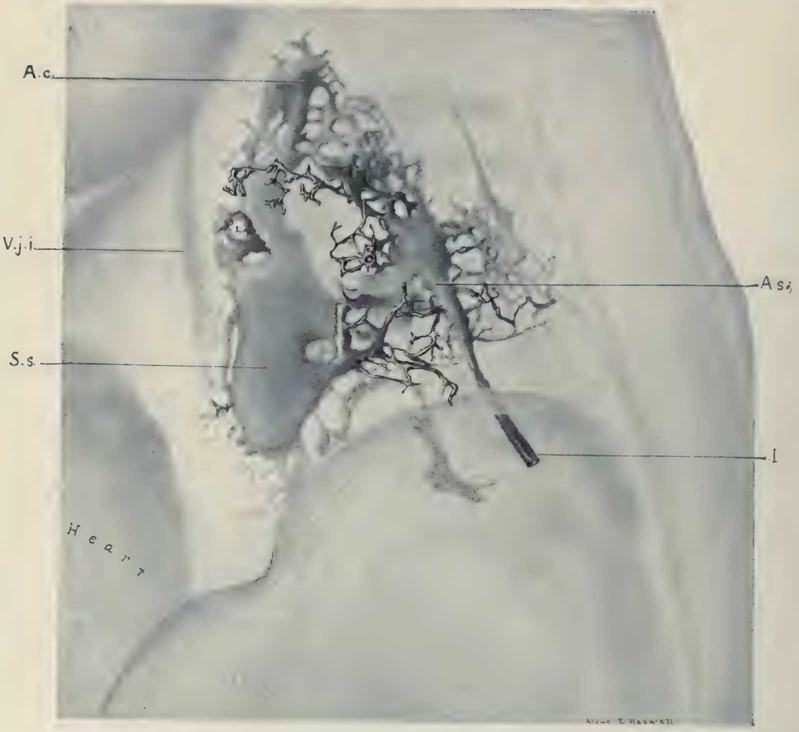

Fig. 7.—Injection of the left jugular lymph sac in an embryo pig which measured 18 mm. in its greatest diameter. The specimen was fixed in 10 per cent formol and cleared by the Spalteholz method. Magnified about 30 times. The glass canula which shows piercing the upper border of the arm bud shows the point of injection. A. c. = anterior curvature of the lymph sac; A. s. = apex of the lymph sac; I. = glass canula used for injection; S. s. = stalk of the lymph sac; V. j. i. = vena jugular interna.

It is not easy to get perfect injections by direct puncture, but by the time the embryo is 16 mm. the dorsal sprouts from the sac are

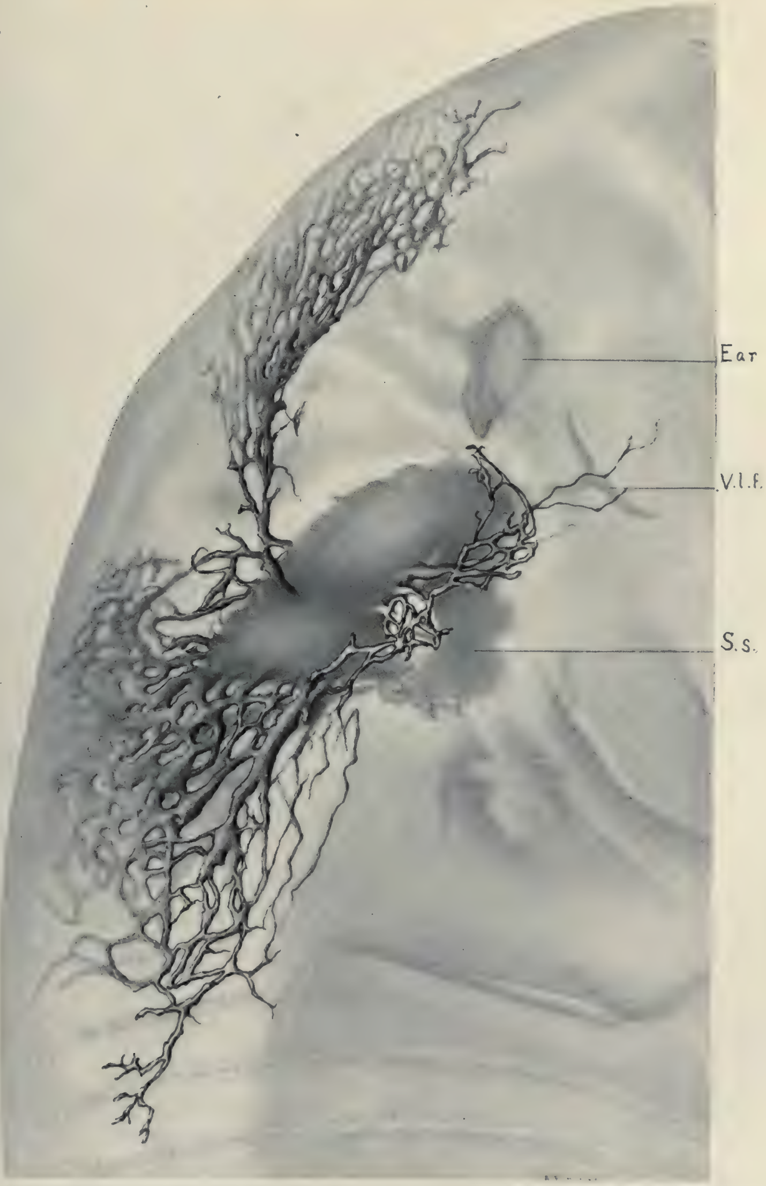

Fig. 8.—Injection of the right jugular lymph sac in fœtal pig measuring 3.5 cm. Magnified about 10 times. After A. H. Clark (24); this specimen was shown as fig. 3 in 130; it has since been cleared by the Spalteholz method so that it shows the relation of the superficial lymph vessels to the jugular sac. It shows a complete injection of the suprascapular and occipital plexuses, but an incomplete injection of the superficial cervical plexus. S. s. = the stalk of the sac showing faintly through the shoulder; V. l. f. = vena linguofacialis.

sufficiently large so that the sac can be injected indirectly through them.

The process by which a lymphatic plexus becomes a sac has been called confluence or cavernization by Ranvier (117-118). He says that when two lymph vessels lie in contact the endothelial wall between them disappears (possibly it is retracted) and thus large sacs develop. It is exceedingly interesting that this process does not take place when lymphatic endothelium rests on venous endothelium, as is the case of the jugular lymph sac.

The most interesting stage in the formation of the jugular sac is shown in fig. 7 from an embryo 18 mm. long. To inject the sac at this stage it is again important to note the plan of the blood capillaries In fig. 6 it will be noted that there is a tiny blood capillary which cuts across the lymphatic area from the superficial plexus to the deeper veins and divides the lymphatic area into two parts, a ventral jugular part and a dorsal part. By the time the embryo is from 16-20 mm. long the path of this slender vessel is occupied by a considerable plexus of blood vessels and by nerves as well. The sprouts from the main jugular sac (fig. 7) have grown up into the dorsal lymphatic area and there developed into an abundant plexus. It is this plexus which can be injected, as is shown by the glass tube which pierces the arm bud. The original sac is shown just lateral to the shadow of the internal jugular vein. This is difficult to inject by direct puncture, because the blood capillary plexus over it has become double and is excessively abundant. Moreover the sac is now just mesial to the developing external jugular vein and lies very close to it. The blood capillary plexus of the groove shown in fig. 6 is now deeper in, and the entire area of the groove so dense a vascular area that no canula can enter the zone without filling the blood capillaries. But just ventral to the groove in the dorsal lymphatic area almost every puncture will fill the lymphatics, provided it avoids the superficial blood capillaries. This dorsal lymphatic area is destined to be the posterior triangle of the neck; even in this early stage it looks translucent and continues to do so, for it is always uncovered by muscle, lying between the trapezius and the sternocleidomastoid muscles (fig. 17).

A description of the form of the sac in fig. 7 will make the basis for the description of the peripheral lymphatics of the head, neck and thorax worked out by A. H. Clark (24) and given in section V. The primitive sac is the portion above the arm bud and lateral to the internal jugular vein. This becomes the internal jugular trunk; the cerebral end of this portion is an abundant lymphatic plexus, the anlage of a single gland in the pig (A. H. Clark) which drains the pharynx. In the dorsal lymphatic zone the rest of the sac is a complete arch from which develop the lymphatics of the shoulder, head, neck, face, arm and thorax. The dorsal arch of the sac becomes by far its largest portion, as will be readily seen in fig. 8, from an embryo 3.5 cm. long. This is the same specimen shown as fig. 3 (Sabin 130). It has since been cleared by the Spalteholz method, so that it shows the sac as well as the superficial lymphatics.

The transition stages between fig. 7 and fig. 8 are very easy to inject and can be readily imagined. The further development of the sac, especially with reference to the lymphatics along the external jugular vein, is brought out in the sections on the peripheral lymphatics and glands.

C. THE RENAL SACS.

The study of the rest of the lymph sacs in the pig may well begin with the interesting and valuable work of Silvester (140). Silvester has shown that in the monkey all of the lumbar and mesenteric lymphatic ducts drain not by the thoracic duct into the jugular veins, but directly into the renal veins or the surface of the inferior vena cava near the renal veins. This he shows in a number of figures from beautiful injections.

A. RETROPERITONEAL SAC.

It had previously been discovered by Lewis (76) in a study of rabbit embryos that a lymphatic sac develops just ventral to the median mesonephritic vein. Baetjer (8) proved that this, the retroperitoneal or præ-aortic sac, arises from the ventral surface of the large vein which connects the two Wolffian bodies in embryo pigs measuring from 17 to 23 mm. long. Baetjer's fig. 3, from an embryo 19 mm. long, shows the blood-filled lymphatic buds which have been slightly injected from the veins. These buds rapidly form a large sac which lies in the root of the mesentery and is the place of origin for all of the mesenteric lymphatics (Heuer, 43); those that grow to the stomach and intestine, the liver, the capsule of the Wolffian bodies and the reproductive glands. The blood-filled lymphatic buds can be seen in the fresh embryo pig 19 to 20 mm. long, if the intestine is pushed to the side and the veins are emptied of blood by injecting them with salt solution.

The retroperitoneal sac becomes the largest of all the lymphatic sacs in the pig. As shown in Heuer's fig. 3 (43) it spreads out just behind the rectum and covers the entire area in the root of the mesentery between the two Wolffian bodies. It spreads over the ventral surface of the Wolffian bodies as far as the edge of the reproductive glands. It was from injecting this sac that Heuer was able to study the development of the lymphatics of the intestine.

This sac would give an excellent opportunity to study the process of cavernization. Injections of it with silver nitrate give beautiful specimens, showing the endothelial-covered trabeculæ that cross its lumen. Total preparations of the silvered sac remind one of the trabeculæ in the wall of the cavity of the heart. These trabeculæ, which are the beginning of the process of transferring the sacs into lymph glands, show especially well in sagittal sections of pig embryos 20-25 mm. long.

2. Iliac Sac—Cisterna Chyli.

I can now bring some evidence to show that the iliac lymphatics which drain the legs, tail and abdominal wall, and the cisterna chyli which forms the lower part of the thoracic duct, arise together as buds from veins of the Wolffian bodies. A complete account of this process needs a more extensive illustration of the blood vessels of the region than I can give at this time. In the pig the lymphatics which bud off from the veins of the Wolffian body and grow forward dorsal to the aorta to form the cisterna chyli and caudalward along the edge of the Wolffian body to form the iliac lymphatics, do not begin until the embryo is 22 mm. long. I found that they arise from the mesonephritic veins because a direct puncture of the blood-filled buds entered the main veins and not the blood capillaries. In a litter of pigs which measured 23 mm. I washed out the blood vessels with Locke's solution, and then opened the specimens and pushed one of the Wolffian bodies over toward the midline. A plexus of blood-filled lymphatics was then readily seen dorsal to the aorta. I succeeded in puncturing some of the larger vessels of the plexus forming the cisterna chyli in three specimens and saw the ink run from the lymphatics into the mesonephritic veins. In all of these injections the cisterna chyli is obscured by extravasations at the point of injection, but they all show the iliac lymphatics. For the present I shall describe the renal lymphatics from sections which can be done in the blood-packed stage.

The description of the iliac lymphatics, however, needs an outline of the blood vessels of the region. If the veins of the prevertebral space between the level of the median vein connecting the Wolffian bodies and the root of the tail be injected it will prove that they are enormously abundant. In the embryo measuring 20 mm. the segmental veins draining the cord and the body wall make an extensive network, which drains in part into the median vein of the Wolffian body and thence directly to the vena cava, while farther caudalward this same plexus drains directly into the large surface

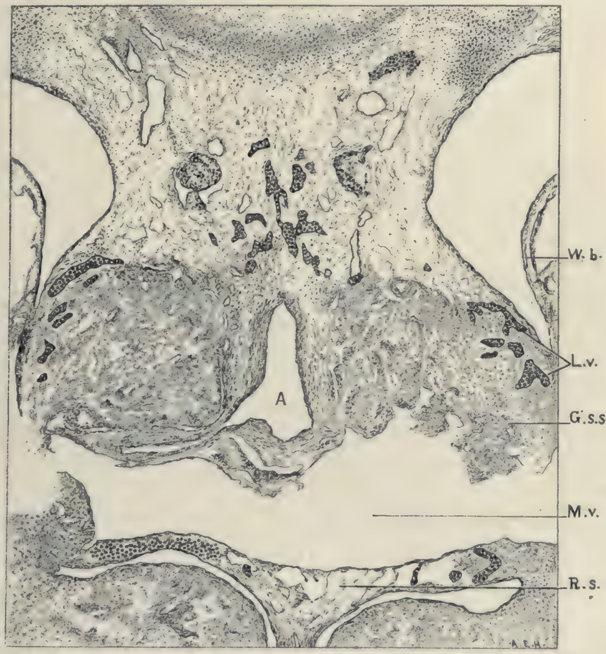

FIG. 9.—Section through the hilus of the Wolffian bodies to show the place of origin of the iliac lymphatic vessels and the abdominal part of the thoracic duct in an embryo pig 23 mm. long. (Specimen 23b.) Magnified 50 times. A. = aorta; G. s. s. c. = gl. suprarenalis s. corticalis; L. v. = lymph vessels filled with blood; M. v. = vena mesonephritica; R. s. = retroperitoneal lymph sac, a part of which is filled with blood, a part empty; W. b. = edge of the Wolffian body.

veins of the Wolffian body. Opposite the lower pole of the Wolffian body this plexus is directly continued into the iliac veins. Cross sections of injected embryos at this stage, namely, 20 mm., show that the entire area lateral to the aorta and between the two Wolffian bodies is practically filled with a plexus of these segmental veins. By the time the embryo is 22 or 23 mm. long, however, there is a small non-vascular area along the dorsal-medial edge of the Wolffian bodies, and into this small area the iliac lymphatics bud. The earliest specimen in which I have found these blood-filled buds measures 22 mm.; the specimen is of interest because it shows clearly that the buds lie against the veins of the Wolffian body itself as well as the median mesonephritic vein. The place of origin of the cisterna chyli and iliac lymphatics can be best seen in fig. 9, which is a cross section of an embryo measuring 23 mm. through the median mesonephritic vein. Just lateral to the aorta are the masses of the sympathetic nervous system through which runs the great plexus of the segmental veins, and the cortex of the adrenal bodies. Ventral to the aorta is the mesonephritic vein, and the retroperitoneal sac, some of the buds of which are full of blood and some now partly empty. In the dorso-medial edge of the two Wolffian bodies is the plexus of blood-packed lymphatic buds which arches across the midline, and, as shown in fig. 10, which is farther cerebralward, forms a definite blood-filled cisterna chyli in the midline.

My various series of cross sections of pigs of about the same measurement are interesting, because they show the progression of the buds. In a specimen (23a) the iliac lymphatics extend only as far as the hilum of the permanent kidney which lies dorsal to the lower pole of the Wolffian bodies. The iliac buds lie throughout their course in the same relative position to the Wolffian bodies and the aorta as is shown in fig. 9. In this specimen (23a) the iliac lymphatic plexus is spreading over the capsule of the permanent kidney, showing that it receives lymphatics while they are in the blood-filled stage. In later stages I have injected lymphatics from the iliac sac around the pelvis of the kidney. It is thus clear why the lymphatics of the kidney drain into the iliac lymph glands, while those of the reproductive glands which develop ventral to the Wolffian body drain into the præ-aortic glands. In a series 23b from the same litter as 23a the iliac plexus is complete, extending from the mesonephritic vein to a dilated sac opposite the bifurcation of the aorta. It was this swollen end of the iliac lymphatics that I identified in embryos 25 mm. long and called the posterior sac in 1901 (Sabin 129). The space for the iliac chain in the pig is small, much smaller than in human embryos, and the iliac vessels in the pig are therefore very inconspicuous in cross sections, except in the blood-filled stage. They can be found, however, when one knows that they lie between the segmental veins and the dorso-medial edge of the Wolffian bodies or kidneys. Sagittal sections are, however, brilliant for the iliac lymphatics and cisterna chyli in the blood-filled stage. In a sagittal series of a specimen 23 mm. one can see the entire iliac chain in a single section, from the mesonephritic vein to the blood-filled sac just caudal to the Wolffian body. From this caudal swelling, from which a large group of iliac glands develops in the pig, three sets of vessels grow out: (1) a plexus which completely surrounds the umbilical arteries, (2) the femoral vessels, and (3) the ileo-inguinal vessels.

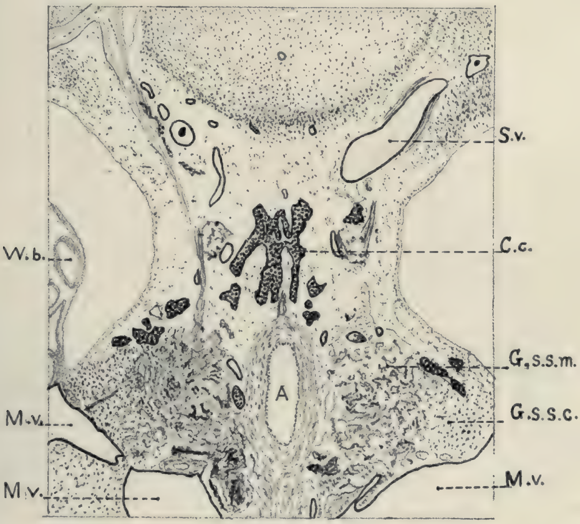

Fig. 10.—Section through a plexus of vessels filled with blood which marks the beginning of the cisterna chyli in an embryo pig 23 mm. long. (Specimen 23b.) Magnified 40 times. The lymphatics are filled with blood, the blood vessels are empty. A. = aorta; C. c. = cisterna chyli; G. s. s. c. = Gl. suprarenalis s. corticalis; G. s. s. m. = Gl. suprarenalis s. medullaris; M. v. = vena mesonephritica; S. v. = segmental vein; W. b. = edge of the Wolffian body.

D. THE THORACIC DUCT IN THE PIG.

The thoracic duct is easy to inject after it is once fully formed, but in the early stages exceedingly difficult. In later stages it can be injected indirectly either from the retroperitoneal sac or from the iliac sac. Moreover it lies in the edge of the wall of the aorta, which guides the needle for a direct injection. In the lower thoracic region it forms such an abundant plexus around the aorta that if the needle avoids the azygos vein it is almost certain to enter lymphatics. Pensa's (105) series of injections in different forms, as well as fig. 7 (Heuer 43), show that it is a constant characteristic of the lower thoracic part of the duct to be a complete plexus around the aorta, while the upper thoracic portion consists of one or two ducts.

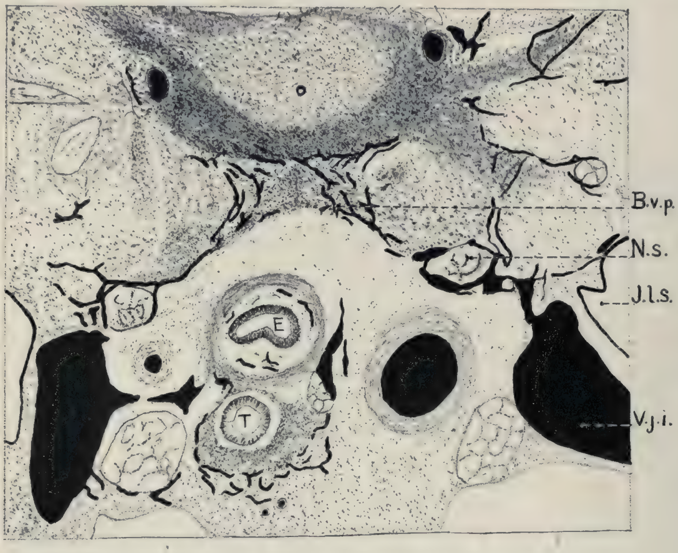

Fig. 11.—Section through the 7th cervical vertebra of an embryo pig measuring 19 mm. Magnified 45 times. The blood vessels have been injected with India ink through the umbilical arteries. This is the stage just preceding the development of the thoracic duct. B. v. p. = plexus of blood vessels ventral to the vertebra; E. = esophagus; J. l. s. = jugular lymph sac; N. s. = nervus sympatheticus; T. = trachea; V. j. i. = vena jugularis interna.

The thoracic duct forms from two places: (1) a duct which grows downward from the left jugular sac, and (2) a plexus which buds out from the mesonephritic veins and completely surrounds the aorta.

Before the thoracic and renal segments have met, however, it is most difficult to inject them.

The early jugular trunk I have never injected directly and only once indirectly from the jugular sac. It will be readily seen that ink injected into the jugular sac usually takes the line of least resistance, the physiological path into the veins. Once in an embryo 23 mm. long I filled the sac, and on pressing the head forward the ink shot into the thoracic duct. The pressure obviously could not be regulated. In 1911 I reported this specimen (23a) at the meeting of the American Association of Anatomists in connection with an unfinished study of the thoracic duct. Dr. McClure requested the specimen for Mr. Kampmeier, who was also studying the thoracic duct in the pig at

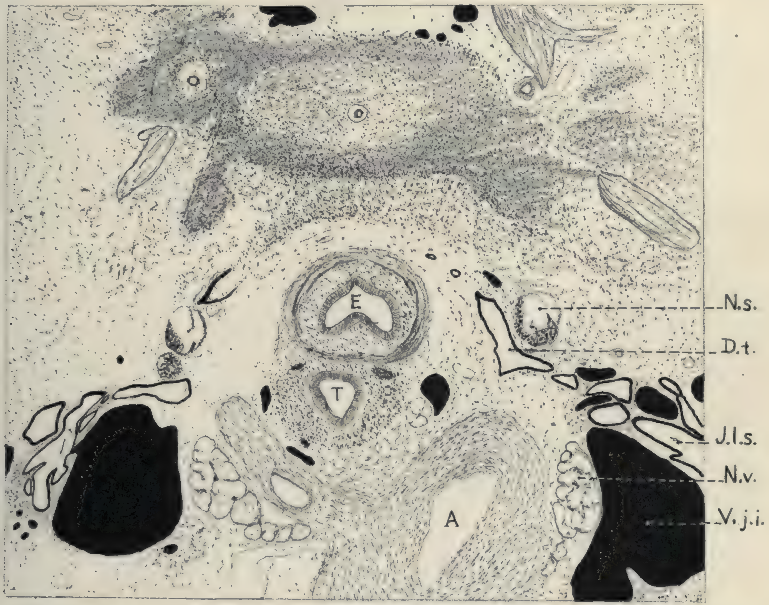

Fig. 12.—Section through the point of origin of the jugular part of the thoracic duct in an embryo pig 23 mm. long. (Specimen 23a.) Magnified 40 times. The left jugular lymph sac and the beginning thoracic duct emptying into it were injected in the specimens; in the drawing the veins are arbitrarily shown as injected and the lymphatics as empty. The thickness of the endothelial lining of the lymphatics has been exaggerated. A. = aorta; D. t. = ductus thoracicus; E. = esophagus; N. s. = nervous sympatheticus; N. v. = nervus vagus; J. l. s. = jugular lymph sac; V. j. i. = vena jugularis interna.

the time, and he has published, with my permission, a valuable reconstruction of my specimen in the Anatomical Record for 1912 (Kampmeier 66).

The thoracic duct needs to be considered in relation to the veins of the region. Fig. 11 is a section through the seventh cervical vertebra of an embryo pig 19 mm. long, which is before the thoracic duct begins. There is a complete vascular injection. It will be seen that there is a vascular zone ventral to the vertebra, and from this zone veins surround the sympathetic nerves and enter the dorso-medial border of the internal jugular vein. The esophagus has a plexus of blood vessels in the submucosa, but dorsal to the esophagus is a non-vascular zone of loose connective tissue. The jugular stem of the thoracic duct grows into this non-vascular area dorsal to the esophagus, as is shown in fig. 12 from 23a. In this tracing of the section the veins are arbitrarily made black and the lymphatics are shown empty, though in the section the left lymphatic sac and its ducts were injected. The thoracic duct lies in the margin of the vascular zone. As Kampmeier's reconstruction of this specimen shows, there is a considerable plexus of lymphatics dorsal to the esophagus near their place of origin from the jugular sac. This plexus connects with the left jugular sac in three places. From the injected plexus a short duct follows the left cardinal vein and I think grows to the heart and lungs. A longer vessel crosses to the right side and is the jugular segment of the thoracic duct. This crossing of the duct behind the aorta I have frequently, though not always, noted in older stages.

The right lymphatic duct curves ventralward and grows to the heart and lungs. Its course is shown in fig. 13 for an embryo 25 mm. long. The asymmetry of the thoracic duct is confined to the jugular portion and corresponds with the asymmetry of the aorta. It is interesting to note that Sala (137, Taf. 14, Fig. 16) and Pensa (104, Taf. 15, Fig. 2) picture a symmetrical thoracic duct in the bird.

The position of the cisterna chyli has already been shown in figures 9 and 10. The cisterna chyli and lower part of the thoracic duct arise in common with the iliac sacs from the mesonephritic veins on either side, as shown in fig. 9. These lymphatic buds from the two sides meet dorsal to the aorta and grow both cerebralward and caudalward along the dorsal wall of the aorta. This makes an abundant plexus of blood-filled lymphatics along the course of the abdominal aorta. Any sections of pig embryos of this stage will show that the veins around the aorta are very abundant, so that the non-vascular space is small. Just opposite the adrenal anlage, however, there is a transition zone which is less vascular. It marks the end of the azygos veins. Below this level the segmental veins drain through the Wolffian bodies, and here the lymphatics form a wider plexus, which becomes the cisterna chyli, fig. 10. As in the adult there is a gradual transition between the cisterna chyli and the rest of the aortic plexus, both the part which extends caudalward and the part which extends cerebralward. Figure 10 shows the cisterna chyli while it is still a plexus and not a sac. The series shows that in many places this dorsal plexus of lymphatics is sending sprouts around to the ventral præaortic sac. All of the abdominal sacs, the retroperitoneal, ventral to the aorta, the two lateral iliac sacs and the dorsal plexus connect with

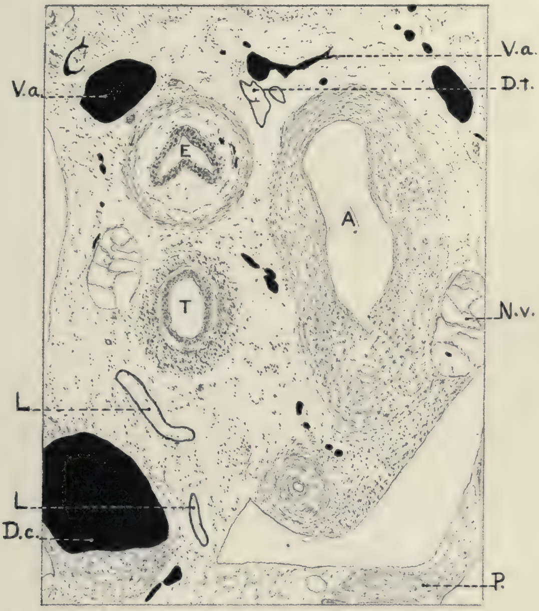

Fig. 13.—Section through the upper thoracic region of an embryo pig measuring 25 mm. in which the blood vessels are injected, to show the vessels of the right lymphatic duct approaching the heart. Magnified 40 times. The injection of the blood vessels was made through the umbilical artery. A. = aorta; D. C. = duct of Cuvier; D. t. = ductus thoracicus; E. = esophagus; L. = lymph vessels to the heart from the right lymphatic duct; N. v. = nervus vagus; P. = pericardium; T. = trachea; V. a. = vena azygos.

each other. In following the series cerebralward from the level of fig. 9 it is clear that the blood-filled lymphatics not only arch across the midline dorsal to the aorta, but they follow the border of the Wolffian bodies lateral to the aorta. Above the adrenal bodies the Wolffian bodies approach very close to the aorta, and some of the lymphatic buds curve around the ventral surface of the aorta. Thus in a specimen 23 mm. long there is a plexus of blood-filled lymphatics surrounding the aorta and extending into the lower thorax as far as the cerebral pole of the Wolffian bodies. At the cerebral end of the Wolffian bodies there are large veins which curve ventral to the aorta and connect the veins of the capsule of the Wolffian bodies. Some of the lymphatics are near these median veins.

The finding of the renal lymphatics in the blood-packed stage makes it quite certain that the thoracic duct arises in two places: First, the jugular stem, which can be injected from the left jugular sac and develops long after the jugular sacs are entirely empty of blood; and, secondly, the renal plexus, which surrounds the aorta and forms a definite cisterna chyli.

These two observations, namely, (1) the presence of blood in one part and its absence in the other, and (2) the fact that injections prove a connection of the jugular stem with the jugular sac, and of the abdominal plexus with the mesonephritic veins, make it quite certain that the two portions of the thoracic duct are distinct from each other in embryo pigs measuring 23 mm., and hence that the thoracic duct begins in two places. Practically the entire question at issue between those of us who think that the lymphatics grow by their own endothelial wall and those who do not centers around the question of how the thoracic duct develops, or, to put it more specifically, how these two lymphatic anlagen become connected. The discussion centers around my specimen 23a, which Kampmeier studied and which he uses as his most conclusive evidence of the theory of the growth of lymphatics by the addition of tissue spaces. On the other hand, it is my theory that the thoracic duct grows from these two anlagen from the veins by the same method by which other lymphatic capillaries can be seen to grow in a living specimen, namely, by the sprouting of their endothelial wall. It is true that I have not yet sufficiently mastered the difficulties of injecting the renal lymphatics to demonstrate the progression of the thoracic duct and indeed it may not prove possible to get as conclusive proof of the origin of the deep lymphatic sacs as of the more superficial ones; yet the inference that they arise in the same manner is in harmony with our modern knowledge of morphology. I wish to postpone a discussion of Kampmeier's evidence until I have described the thoracic duct in a human embryo, and discussed the development of the theories opposed to my own—of which Kampmeier's work is a part (Sec. VIII).

2. PRIMARY LYMPHATIC SYSTEM IN HUMAN EMBRYOS.

On this description of the lymphatic system in one mammalian form I shall base an account of what is known of the primary system in other forms. All of the primary lymphatic sacs have been found in the human embryo. The jugular sac is the earliest to appear. It has been found as a few blood-packed buds in two embryos measuring 8 and 9 mm. (Mall collection, No. 397 and No. 163, Sabin 134.) They are on the lateral surface of the anterior cardinal vein near the duct of Cuvier and were described as veins (Sabin 133, 134), since at that time the blood-filled buds were thought to be blood capillaries. The blood-packed buds extend along the lateral surface of the anterior cardinal vein and very early develop sprouts that project dorsalward. These are plain in an embryo measuring 11 mm. (Mall collection, No. 353, figs. 7 and 8, Sabin 133, and figs. 490 and 491, Sabin 134.) The figures of this specimen, together with the reconstruction of Lewis (Harvard collection No. 1000, measuring 16 mm.; No. 189, measuring 11.5 mm.; and No. 1322, measuring 16 mm., figs. 1-3, Lewis 78), show that the jugular lymphatics in the human embryo not only bud from the anterior cardinal veins, but from the posterior cardinal vein, and the common stem or plexus which forms the origin of the primitive ulnar and thoraco-epigastric veins. A large extension of the jugular sac along the primitive ulnar vein is characteristic of human embryos (fig. 12, Sabin 133, or fig. 493, Sabin 134, and figs. 2 and 3 after Lewis 78).

In a human embryo 10.5 mm. long I have found a small sac only partly filled with blood (figs. 3-6, Sabin 133, and figs. 488, 489, Sabin 134). This specimen has also a beginning thoracic duct. These two facts show that there is considerable variation in the rate of growth of the lymphatic system of different specimens.

The study of human embryos has also brought out the fact that the openings of lymphatics into the veins can only be made out when the section happens to be cut in the right plane for each valve. For the jugular sac frontal sections are the best (figs. 492, 494, Sabin 134).

A new embryo in the Mall collection, No. 460, measuring 21 mm., is of great interest in connection with the renal lymphatics. A careful reconstruction of this specimen with abundant illustrations would be of value, but for the present I can give only a description. I injected the embryo with India ink into the umbilical artery while the heart was still beating. The vascular injection is almost perfect. The embryo was then put directly into bichloride-acetic and the fixation is excellent.

In marked contrast to the embryo pig of about the same length, the Wolffian bodies are disappearing, being pushed caudalward by the growing permanent kidneys. The cerebral pole of the Wolffian bodies lies far to the side opposite the median mesonephritic vein which, as Baetjer (8, fig. 7) shows, connects the Wolffian bodies opposite their hilum in embryo pigs measuring 20 mm. This median vein in the human embryo (No. 460) passes over the ventral surface of the adrenal bodies and still receives the veins of the cerebral pole of the Wolffian bodies. It also receives a plexus of veins from the permanent kidneys. It is markedly asymmetrical on account of the development of the vena cava on the right side.

Blood-filled lymphatic buds completely surround this mesonephritic vein in the midline, making the anlage of the retroperitoneal or præ-aortic sac; some of those that come from the dorsal surface of the vein have pushed between the masses of the sympathetic ganglia and reached the dorsal surface of the aorta. In some sections, the retroperitoneal buds are partly emptied of their blood. The area at the root of the mesentery opposite the median mesonephritic vein is small in the human embryo as compared with the corresponding area in the pig and the retroperitoneal sac is correspondingly small.

The iliac sacs and the beginning thoracic duct are also present. Along the dorso-medial wall of the kidney in the angle between the segmental veins and the plexus of renal veins are two long iliac sacs. They are evidently farther advanced than the retroperitoneal sac, for they are nearly empty. The one on the left side measures 1.8 mm. and extends to the bifurcation of the aorta. On the right side the empty sac is considerably shorter, but its lower part is replaced by blood-filled buds along the inferior vena cava.

In tracing the lymphatics cerebralward, from the level of the hilus of the kidney, there is a small lymphatic capillary plexus in the place of the cisterna chyli and the two lateral sacs become a plexus of small ducts which can be traced the entire length of the permanent kidneys and then along the dorso-lateral surface of the aorta, just ventral to the azygos veins. This small plexus of ducts is nearly empty on the left side, but full of blood on the right side. The two plexuses can be followed almost to the level of the bifurcation of the trachea. Some blood in the plexus on the left side just before the vessels end makes it possible that the renal part of the thoracic duct does not yet connect with the jugular part of the duct.

This particular specimen is interesting in regard to certain zones of dilated tissue spaces which are conspicuous along the aorta. There are some of these large spaces near the bifurcation of the aorta, in the root of the mesentery near the retroperitoneal sac, and along the ventral surface of the aorta, especially opposite the mesentery of the stomach and opposite the bifurcation of the trachea. I have studied them with care to see if they have any definite relation to the developing lymphatics and am sure that they have not. Sometimes they are near the lymphatics and sometimes not. Those in the thorax are not adjacent to the lymphatic plexus. They can be distinguished from the endothelial-lined lymphatics, but if one were convinced that lymphatics came from tissue spaces one might imagine transition pictures between the tissue spaces and the ducts. This is particularly true when the endothelium of a lymphatic vessel sags away from the surrounding tissue, a picture familiar to histologists in sections showing lymphatics in adult tissues. The further discussion of the thoracic duct is in part VIII.

All of the primary lymphatic system is present in a human embryo measuring 30 mm. (Mall collection No. 86, fig. 12, Sabin 133, copied as fig. 493, Stricker 144). This stage represents the maximum size of the jugular sac. The dorsal arch is large and its line of separation from the jugular part is indicated by the perforation for the cervical nerves and blood vessels. The very small mesenteric sac and larger iliac sacs are distinct as well as the complete thoracic duct.

3. PRIMARY LYMPHATIC SYSTEM IN RABBIT EMBRYOS.

In 1906 F. T. Lewis (76) published a valuable paper on the lymphatic system in rabbit embryos. Besides excellent reconstruction of the primary lymphatic system in rabbits, the cat and the pig, this paper has three important points: First, the discovery that the early lymphatics are filled with blood, which has proved to be of such value, now that its meaning is understood. Second, the discovery of the retroperitoneal sac which he described as lying adjacent to the mesenteric veins. He also showed the iliac sacs and cisterna chyli; all of which we now know come from the renal veins (Sabin 136). Third, he noted that lymphatic ducts when they are reconstructed from sections appear as a row of beads. Since these rows of beads occurred along the veins in his reconstructions and since he could not find the connections of the early sacs with the veins he was led to suggest that lymphatics might arise from multiple anlagen split off from the veins along their course. The apparently isolated endothelial-lined vessels found in serial sections we call Meyer-Lewis anlagen. They are discussed in section VIII.

The jugular sac in rabbits has an early extension along the primitive ulnar vein like that of the human embryo. The dorsal portion of the sac, for the posterior triangle of the neck, arises from a large stalk from the primary jugular portion between the level of the 4th and 5th cervical nerves.

4. PRIMARY LYMPHATIC SYSTEM IN THE CAT.

The primary lymphatic system in the cat will be described from the extensive work of Huntington and McClure (51-58 and 91-94), one reconstruction of Lewis (76) and a few injections of my own. The work of Huntington and McClure has been mainly on the development of the jugular lymph sacs and the thoracic duct in the cat and their observations are for the most part brought together in two extensive papers (54 and 58). Their work is difficult to analyze and cannot be done entirely accurately without seeing their sections. They have relied on the appearances of sections and the appearances of wax models from them to differentiate lymphatics, and since these are not adequate criteria it is impossible to be sure that all the structures shown as lymphatics are lymphatics; in fact, one can be certain that some of them are not. Their theories in regard to the origin and development of the lymphatic system are discussed in sec. VIII. In the article (54) on the jugular lymph sac of the cat figs. 8 to 21 may be disregarded as evidence, since they are diagrams. Figure 22, which they group under "Early Venous Stages," is, I think, a reconstruction of the cardinal veins before the lymphatics begin (and is therefore to be compared with Evans' (34) fig. 3, and with my fig. 4 in this paper). In their fig. 22 the fourth segmental vessel is shown and described (page 226) as "formed by the confluence of two extended para-neural channels." This is intended to indicate the beginning of the lymphatics, but since their fig. 43 from an embryo 10 mm. long shows undoubted lymphatics in the blood-packed stage, I think it is practically certain that the specimen measuring 5 mm. does not show lymphatics. It is not necessary to prove that veins do not open into the tissue spaces around nerves.

The description of the stages between 5 and 10 mm. is bound up with the discussion of "fenestration." In reconstructing the veins Huntington and McClure have noted the pattern of the developing veins, which is especially well shown in fig. 4, in connection with the pericardial veins. In this specimen the pericardial veins drain into a loop which connects the anterior cardinal vein with the duct of Cuvier. The formation of this loop is a part of the process by which the pericardial veins shift from the duct of Cuvier to the anterior cardinal vein. Numerous small loops are seen along the anterior cardinal veins in figs. 4 and 5. They are characteristic of the veins. They suggested to Huntington and McClure a vague conception of a relation to the lymphatics which they expressed as follows (p. 204 in 54): "In a subsequent stage confluence of these 'fenestræ' results in the more or less complete separation of the primary vein into two parallel secondary channels, which appears to be a uniform principle in the development of parallel venous trunks. Or, as in the case of the jugular lymph sac, further extension of the same process may result in separating from the main venous channels elements which unite to form a closed sac entirely distinct from the vein from which it arose. The term 'fenestration' means, therefore, in the sense in which it is employed in this paper, one of the last stages in the definite crystallization of the venous system out of an indefinite antecedent plexiform condition, and the determination of an important element in lymphatic organization, closely associated with the embryonic venous system." The lymphatics which they thought formed by this process they termed "veno-lymphatics." Both terms "fenestration" and "veno-lymphatics" should drop out; there are no veno-lymphatics, for the lymphatics bud directly from the veins as lymphatics, and fenestration is a term that describes models better than the actual process of growth by sprouting by which the veins are formed.

Some of the figures of the models from embryos measuring 7 mm., for example fig. 33, represent lymphatics in the early plexus stage; I do not, however, find any mention of the presence of blood. Figure 46 shows the beginning of the enlarging of the plexus into sacs. From their later stages figs. 46 to 65, but much better from Lewis, fig. 6 (76), can be made out the especial characteristics of the jugular sacs in the cat. They are (1) that the jugular sac in the cat arises from the posterior cardinal vein as well as from the anterior cardinal vein. This point is well shown in Huntington and McClure figures. (2) The cerebral end of the ventral or jugular portion of the sac is very large. This is the part that drains the larynx. (3) The internal jugular trunk is small. (4) The dorsal apex of the sac which lies in the posterior triangle of the neck is large. (See Lewis' fig. 6.) It is connected with the cerebral end by a slender vessel. In injections of the sac in embryos between 30 and 60 mm. long it looks very much like the sac in a bovine embryo as shown by Polinski (107) in his fig. 7. It lies nearer the arm than the corresponding portion of the sac in the pig. (5) There is a large extension though possibly a distinct sac (Lewis, fig. 6) along the primitive ulnar and thoraco-epigastric veins. This sac is very conspicuous in older stages, extending into the axilla and receiving large trunks from the thoracic wall. This makes the jugular lymphatic sac in the cat more like the human than the pig (sec. V).

The segmental divisions of the sac as indicated by colors in the Huntington and McClure figures are arbitrary and not as valuable as the divisions I have just given, which correspond to the function of the different glands which develop from the sac.

Lewis' figure also shows a very interesting view of the retroperitoneal and iliac sacs as a continuous plexus, which again emphasizes the fact that the renal sacs anastomose with each other.

5. Primary Lymphatic System in Birds, Posterior Lymph Heart and Jugular Lymph Sac.

The history of our knowledge of the lymphatic system in birds is most interesting. The early discoveries of the posterior lymph hearts by Panizza, A. F. J. Mayer, and Stannius, as well as the work of

Budge on the relation of the heart to the allantoic vessels, have already been given. From that time on there was no advance until the work of Sala (137), who studied the development of the posterior lymph hearts and thoracic duct. He described the posterior lymph hearts as arising in relation to the lateral branches of the first five coccygeal veins, during the seventh day of incubation. We now know that the posterior lymph hearts bud from the veins during the 5th day (E. R. and E. L. Clark, 29), so that Sala was describing the transformation of the plexus into the sac. He noted the connections with the veins but described the sac as arising from excavations in the mesenchyme. His work, published a short time before my paper on the origin of the lymphatic system from the veins (Sabin 129), was an advance over the preceding work, for it placed the first lymphatics near the veins instead of in the periphery. Sala figured the thoracic duct in the bird as a symmetrical structure (Taf. 14, Fig. 16), and this is also shown in Pensa (104, Taf. 15, Fig. 2). Sala described the early stages of the thoracic duct as being solid cords of cells. This observation, which has been confirmed by Mierzewski (96), makes it necessary to restudy the thoracic duct in the chick, which is now possible through the great improvement in our methods of injection.

The most recent work on the lymphatic system in birds has been done by Mierzewski (96), Jolly (59), Miller (97) and E. R. and E. L. Clark (27-29).

I have already brought out the fundamental importance of the Clarks' work, showing that the lymphatics bud off from the veins in a non-vascular zone, and show a continuous growth to the periphery. Mierzewski had shown that the early lymphatics grow along the lateral line of the embryo, as shown in his fig. 3. It was these lymphatics which grow to connect the posterior lymph heart with the jugular lymph sac that E. L. Clark observed in their blood-filled stage and which led her to watch the process of budding in the living embryo.

The process may best be described in a quotation from p. 254 (29):

> The first evidence of lymphatics in the tail region of living chicks is the appearance of a number of separate knobs, filled with stagnant blood, a little darker in color than the circulating blood, just lateral to several of the most anterior of the dorsal intersegmental coccygeal veins. The connections with the veins cannot be seen, since the knobs lie between them and the observer, but ink injected into the knobs can be seen to pass directly into the main intersegmental veins. Between the separate knobs no anastomoses can be seen, nor can any be discovered by injection.

Soon after these knobs appear (in about fifty-five minutes), similar ones develop about them which have fine connections with them, thus forming a small cluster. The new ones are located partly on either side of the first and partly superficial to them. Their injection now shows discreet tiny clusters, somewhat like bunches of grapes, connected, as were the earliest knobs, with the same intersegmental veins. These clusters are still separate from one another.

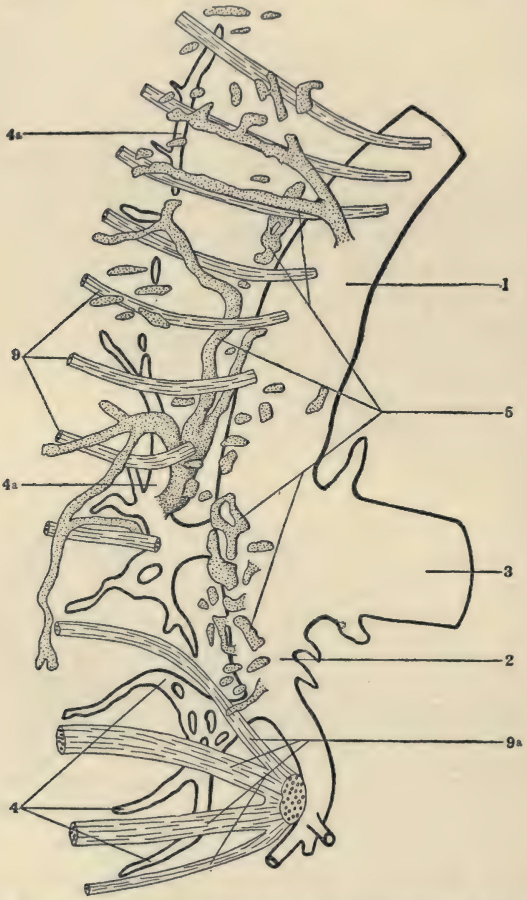

Fig. 14.—After Miller. Diagram from an reconstruction of the veins and nerves of the cervical and upper thoracic regions of a chick embryo 13.5 mm. long, after 5 days and 10 hours of incubation; right side. 1. Præcardinal vein. 2. Post-cardinal vein. 3. Duct of Cuvier. 4. Intersegmental (dorsal) veins. 5. Lateral group of vascular islands and veno-lymphatic vessels. 9. Spinal (cervical) nerves. 9a. Brachial plexus. After Miller, Amer. Jour. of Anat., 1912, Vol. 12, fig. 12.

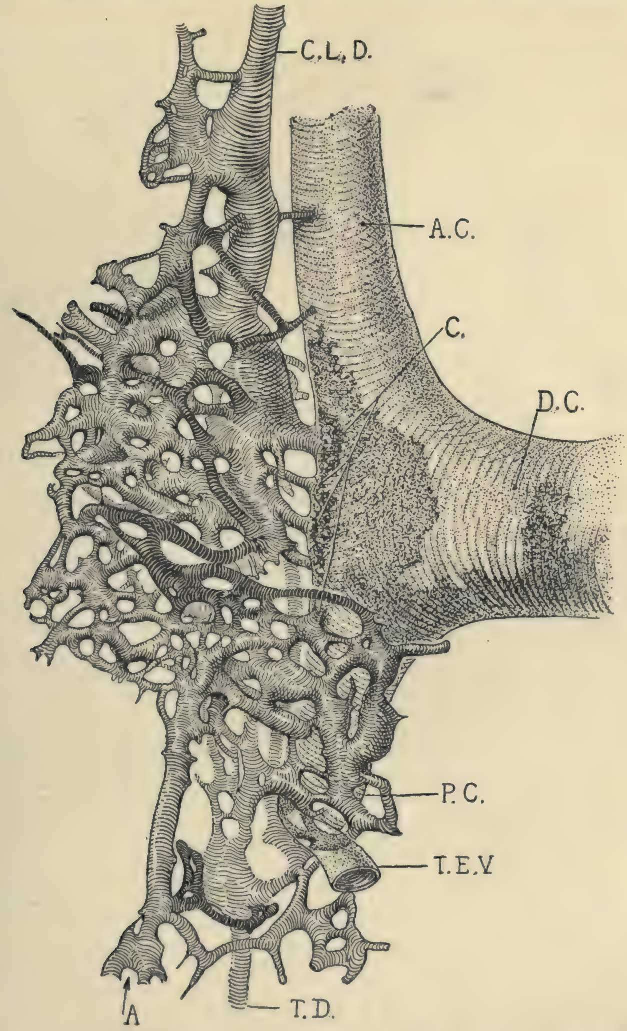

FIG. 15.—After E. L. Clark. Lateral view of the jugular lymphatic plexus of the right side of a chick embryo 14 mm. long after an incubation of 5 days and 20 hours. The measurement was the greatest length and was taken after fixation. With a very fine canula (the lumen of the point being about 15 μ in diameter) diluted India ink was injected under a binocular microscope into one of the superficial lymphatic capillaries in the skin between the fore and hindlegs. From here the ink filled the deep jugular lymphatic plexus, and from there a few granules entered the vein through five connections (C). The drawing was made with the help of a camera lucida with a Zeiss binocular microscope (oculars No. 4, objective A_2). Magnified 67 times. A. = vessel which connected the superficial lymphatic capillaries with the jugular lymph plexus and which was injected; A. C. = vena cardinalis anterior; P. C. = vena cardinalis posterior; D. C. = duct of Cuvier; C. = communications between the jugular lymphatic plexus and the veins; T. D. = deep lymphatic vessel; T. E. V. = vena thoraco-epigastrica; C. L. D. = cervical lymph vessel. After E. L. Clark's fig. 1, Anat. Record, 1912, Vol. 6, p. 263.

There is a rapid extension of these blood-filled structures, and soon, in about an hour and a half after their first appearance, connections between neighboring clusters may be seen. Injection at this stage with India ink shows an anastomizing plexus, connected, as before, with the intersegmental veins. Injection with silver nitrate shows distinct endothelial markings in the walls of the plexus.

During this plexus formation there is a steady extension toward the surface, and by the time anastomoses have formed between neighboring clusters sprouts have grown to the surface and started to extend in the region superficial to the plexus and also ventralwards. It now becomes possible to study with more minuteness the changes which are going on, since these sprouts are quite superficial and are developing in a plane parallel with the surface. Observation and successive records of these sprouts in the living chick reveal a rapid extension ventrally and also anteriorly, accompanied by a plexus formation. Two or three sprouts are seen to lead and soon numerous connections develop between them. Various portions of the irregular plexus thus formed enlarge and become more densely packed with blood which continues to back up from the vein. Then new sprouts grow out in advance and the same process of extension accompanied by plexus formation is repeated. If a single sprout is selected and frequent careful drawings are made the changes are seen to be rapid and striking. The sprout becomes wider and longer. Branches appear, and they in turn increase in width and length. From a branch a connection forms with the original sprout, thus forming a loop. New branches and connections are formed, making a plexus. Branches from neighboring loops or plexuses meet one another and anastomose. The several parts of the plexus are quite irregular in size. Most of the lymphatic vessels are several times as wide as a blood capillary, while some of the connections are as small as, or even smaller, than a blood capillary. Throughout the blood in these new-forming lymphatics is markedly darker in color than the circulating blood.

This work thus corrects the idea that lymphatics are transformed blood capillaries. They bud out from the veins as lymphatics and gradually invade the body as a new type of vessels.

Miller's work (97) on the anterior lymph sac is chiefly valuable in giving an excellent chance to contrast the method of reconstruction with the method of injection in an area where an injection can be obtained. Figure 14 is copied from Miller's fig. 6, and fig. 15 is from an injection by E. L. Clark's (27, fig. 2) of the plexus in the same stage. The points of the apparently isolated islands of lymphatics and the separation of the sac from the veins show by Miller are errors which are cleared up by E. L. Clark's work. The jugular lymphatic plexus is connected with the vein in a number of places and is a continuous endothelial-lined plexus of lymphatics.

The jugular lymph plexus develops into a small sac (Miller's fig. 6) which becomes a single jugular gland. This small, fusiform gland has been studied by a number of observers and has been worked out in all its relations by Jolly (59) in his interesting paper on the lymph glands in buds.

Miller (97, page 489) quotes Mierzewski as having seen rhythmical contractions of the jugular lymph sacs. A reference to Mierzewski's paper, however, will show that he consistently speaks of posterior lymph heart and jugular lymph plexus and his reference to pulsation (page 479) is a confirmation of Sala's observations in the posterior lymph hearts. Miller notes the absence of muscle and the point should be emphasized, because the jugular lymph sac in birds becomes not a lymph heart, but a lymph gland.

The iliac lymphatics in birds are very well brought out by Jolly (59) in his article on lymph glands. He does not consider their origin, but his fig. 15 shows their distribution extremely well, and his fig. 11, pl. XI, gives the exact histological picture of a lymph sac with connective tissue bridges for a bird on the 18th day of incubation. This is the method by which the primary sacs become lymph glands, as is shown in section VI.

6. PRIMARY LYMPHATIC SYSTEM IN AMPHIBIA, ANTERIOR AND POSTERIOR LYMPH HEARTS.

It is not possible at this time to give a complete account of the development of the lymphatic system of the amphibia and reptilia, but enough evidence is at hand to show that the lymphatics are derived from the veins. The remarkable subcutaneous lymph sacs in the frog have always attracted interest and stimulated a curiosity to unravel their development as was brought out by Langer (75) in 1868. Some recent experiments of Abel (1) which combine anatomical and pharmacological methods add to this interest.

Meltzer (95) had published experiments to show that a smaller dose of a drug produced convulsions when injected into a cardiectomized frog than into a normal one. He concluded that the drug traveled through the tissue spaces.

Abel found that a dye, acid fuchsin, when injected into the lymph sacs of a normal frog was distributed widely over the body by the blood vessels. In a cardiectomized frog a small dose injected into the muscle (where there are no lymphatics, only tissue spaces) traveled exceedingly slowly; on the other hand, a small amount of the fluid injected into a lymph sac traveled rapidly, but in a zone limited exclusively to the lymph sacs, according to their anatomical conections. When the dye reached the lymph heart in the cardiectomized frog it was pumped, not through the heart to the systemic vessels, but through the vertebral veins to the nervous system. Thus is explained the marked effect of the small dose. If the lymph hearts were killed the convulsions did not take place.

It has been shown that the anterior lymph hearts of the amphibia bud off from the vetebral veins (Hoyer 49), or in a more primitive position from branches of the earlier segmental veins which are going to form the vertebrals (Knower 74). They develop earlier than the posterior hearts and have been found in R. palustris, R. sylvatica and R. virescens measuring about 6.5 mm., and in R. temporaria and Bufo vulgaris measuring about 4.5 mm. Hoyer noted the presence of blood in the early stages of both anterior and posterior hearts. Knower brings out the fact in connection with the anterior hearts that they lie on the myotomes from which they derive the striated muscle of their wall. This is, I think, a very important point. The particular myotome Knower has shown may vary.

The pulsations of the anterior lymph hearts can be readily seen in the dorsal surface of the tadpole, just behind the pronephros, and thus they can be injected.

From the anterior lymph heart develop two symmetrical vessels, one of which runs forward toward the head, the other backward toward the tail. The posterior duct as described by Hoyer divides into two branches, one running to the tip of the tail dorsal to the myotomes, the other passing back along the ventral margins of the myotomes to form the ventral caudal trunk. It is the branches of these two caudal trunks which have been studied so much in the living specimen. There is also a lateral branch which runs caudalward from the anterior lymph hearts on the lateral surface of the myotomes half way between the dorsal and ventral branches. This lateral trunk subsequently connects with the posterior lymph heart.

Wieliky (153), Jossifov (62-65), and Favaro (36) thought that the posterior lymph heart arose from the dilation of the caudal lymph trunks which grow from the anterior lymph hearts, and Jourdain (61) describes them as being formed by a rapid destruction of connective tissue. Knower and Hoyer, however, have found that they bud off from the posterior vertebral veins considerably later than the anterior lymph hearts, and they have been well worked out by Barański (9). Barański shows that they arise by several buds from the endothelium of the posterior vertebral vein and its branches. His fig. 1 shows particularly well the heaping up of the endothelium so that it looks like a solid mass at the point of origin. Practically nothing is known of the origin of the deep lymphatics in amphibia.

It has thus been shown that the lymph hearts of amphibia arise as buds or sacs from the endothelial wall of segmental veins. They lie on the myotomes, from which they derive the striated muscle of their wall.

The subcutaneous lymph sacs of the anura are secondary structures. This was found out by Ranvier (116) in 1896, and also by Knower and Hoyer. They are derived from ducts which grow from the lymph hearts. They have been comparatively little studied. Hoyer (49) found that the large sac on the ventral surface of the head (sacc. submaxillaris) developed from a branch of a duct from the anterior lymph heart, and that the lateral sacs are derived from the lateral lymph trunks.

This point has been just shown in connection with the sacs of the extremities by Frl. Goldfinger (38), who has injected the primary ducts and then the increasingly denser lymphatic plexus up to the final lymph sacs. This process of cavernization could be studied here by silver nitrate injections.

Since the above was written Hoyer (49a) has published an article in which he gives a general review of the origin of the lymphatic system in vertebrates, and Hoyer and Udziela have given the first comprehensive description of the lymphatic system in a urodele (49b). In a salamander larva the lymphatic system opens into the veins first through symmetrical axillary lymph sacs or sinuses, and secondly through a series of subcutaneous lymph hearts which pump the lymph into the vena lateralis (Meyer 88a and Marcus 87a).

There are six longitudinal lymph trunks, four superficial and two deep (Hoyer 49b, Taf. XII, Figs. 1, 2 and 5). (1) The median, dorsal, longitudinal lymph trunk, which extends from the point of the tail to the middle of the head; (2) a medial, ventral caudal trunk, which branches around the cloaca and opens into the inguinal sinus as is shown in fig. 2 (49b); (3 and 4) symmetrical lateral trunks, which lie external to the myotomes and open in part into the segmental lymph hearts and in part into the axillary sinus, and (5 and 6) the deep subvertebral lymph trunks. The subvertebral lymph trunks are paired vessels with many anastomoses which extend from the tip of the tail to a point opposite the stomach, where they unite to form a cisterna chyli. From the cisterna chyli four vessels run forward to the axillary plexus, the paired thoracic duct and the two paravertebral lymph trunks.

The axillary lymph sacs open by three or four branches into the cardinal veins and receive the following vessels: (1) The lateral superficial lymph trunks; (2) the paravertebral vessels; (3) the thoracic duct; (4) vessels of the cranial part of the stomach and esophagus; (5) a vessel which runs in the groove between the pericardial and peritoneal sacs; (6) a vessel which comes from the base of the skull; (7) superficial vessels from the side of the head, and (8) the lymph vessels of the forelegs.

Besides the axillary sac there are two other sacs or sinuses, one of which lies dorsal to the aorta at the base of the heart, namely, the sinus lymphaticus cordis (Hoyer 49b, fig. 5), and is in the course of the jugular lymph trunks and the other of which makes the paired sinus of the inguinal region.

The segmental lymph hearts receive three groups of vessels: (1) branches from the subvertebral lymph vessels (which agrees with the findings of Marcus 87a, in Gymnophionem; (2) dorsal and ventral segmental branches, and (3) the longitudinal lymph trunk. They open into the vena lateralis. The segmental lymph hearts and the sinus lymphaticus cordis have striated muscle in their walls. It is clear that a knowledge of the origin of this system would be of great value, as Hoyer says: "Erst wenn die berührten noch zweifelhaften Punkte durch weitere Untersuchungen vervollständigt sein werden, wird eine gewisse Grundlage zu vergleichenden Betrachtungen des Lymphgefässystems der niederen Wirbeltiere geschaffen sein" (49b, p. 555).

Stromsen (145) and Huntington (57) have worked on the development of the lymphatic system in reptiles. Stromsen shows that the posterior lymph hearts develop in relation to the coccygeal veins. He describes the process as a combination of veins and dilated spaces similar to Sala's decription for the corresponding hearts in birds. This method of formation has now been disproved by the observation of the process in the living chick. He notes that the striated muscle of the heart comes from the myotomes. Huntington (57) states that in the reptiles there are jugular lymph sacs like those of mammals. The lymph vessels of reptiles he describes as arising from tissue spaces.

V. PERIPHERAL LYMPHATIC SYSTEM.

1. In the Pig.

A. from the jugular lymph sacs.

I shall again base the description of the peripheral lymphatics on the vessels in the pig, since more of the main trunks have been worked out in that form than in any other. The description is taken from the work of A. H. Clark (24), of Heuer (43) and myself.

The development of the jugular sac in the pig has already been given in section IV. A study of the distribution of the lymphatic vessels from the jugular sac must be based on the form of the jugular sac as seen in figs. 7 and 8. In fig. 7 there is a primary sac between the internal and external jugular veins and a complete arch of lymphatic capillaries extending into the dorsal lymphatic area. This entire plexus becomes transformed into the sac, so that, as shown in fig. 8, the sac consists of a stem along the internal jugular vein and a complete dorsal arch. Through following the fate of this sac A. H. Clark divides it into three parts, the sac stalk; the anterior curvature along the internal jugular vein; and the apex, in the posterior triangle of the neck.

The sac stalk becomes the deep jugular lymphatic trunk. It is usually one large vessel, but may give off lymphatics which run directly to the pharynx. The anterior curvature becomes a lymph gland and it sends vessels to the pharynx and Eustachian tube and to the nose.

The apex of the sac, as is seen in fig. 8, becomes the largest part of the jugular sac. This part lies in the posterior triangle of the neck and develops in the pig into one gland, the largest in the neck (Clark 24). This corresponds to the group of glands in the posterior triangle of the neck particularly well shown in Bartels (10) fig. 30 from new born child.

The fact that the jugular lymph sac in the pig develops into two lymph glands and the deep jugular lymphatic trunk is well brought out in fig. 16 from a pig 5.5 cm. long. The sac is shown in the depth and the swollen anterior curvature (deep jugular gland) and apex (gland of the posterior triangle) stand out through the relatively small size of the connecting vessel.

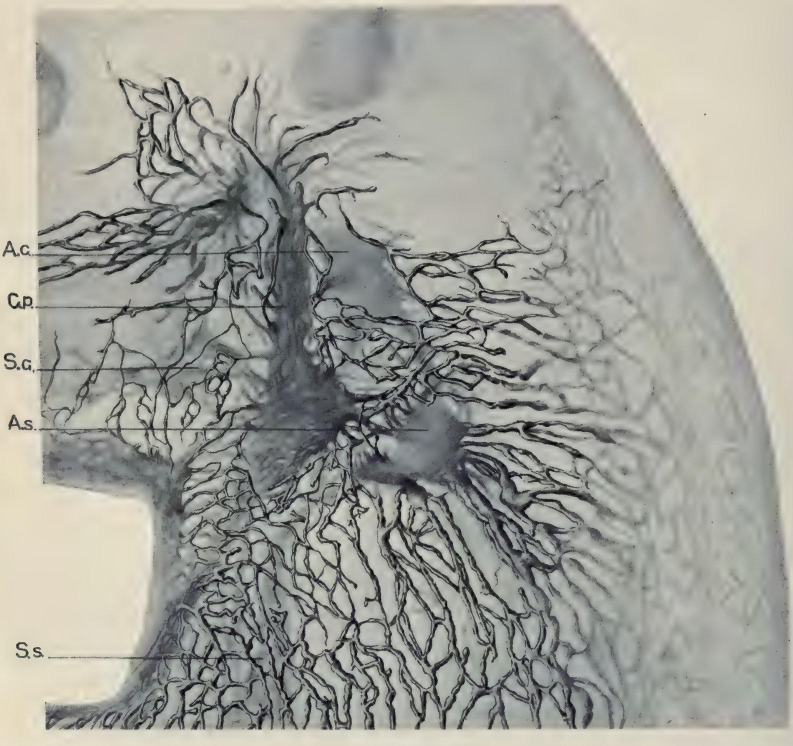

FIG. 16.—Injection of the jugular lymph sac, the superficial cervical plexus, and the superficial lymphatic vessels in the neck of a fœtal pig 5.5 cm. long. After A. H. Clark (24). The specimen was fixed in formalin 10 per cent formol and made transparent by the Spalteholz method. Magnified 7 times. The figure is to be compared with fig. 5 in the Amer. Journ. of Anat., 1904, Vol. 3, p. 118, which shows a complete injection of the superficial lymphatics of the same stage. A. s. = apex of the lymph sac which forms the lymph gland of the posterior triangle of the neck; A. c. = anterior curvature of the lymph sac, which forms the deep jugulo-pharyngeal lymph gland; C. p. = superficial cervical lymphatic plexus; S. g. = lymphoglandular submaxillaris; S. s. = stalk of the jugular lymph sac.

From the apex of the sac superficial lymphatic vessels grow both from the dorsal and from the ventral border. Those from the dorsal and caudal border make a large plexus of superficial lymphatics which, as shown in fig. 8, grow (1) over the scapular region and (2) over the occipital region. The lymphatics from the ventral border of the apex are most interesting and complex. They grow ventralward as shown in figs. 8, 16 and 17 and form a very extensive plexus along the course of the external jugular vein, lateral to the sternocleidomastoid muscle. This is the superficial cervical plexus and it becomes a large group of superficial lymphatic glands in the adult pig (Clark 24).

The cervical plexus not only connects with the apex of the sac, but, as is shown faintly in fig. 16, its caudal end has a group of vessels that connects with vessels that follow the external jugular vein. In a mesial sagittal section of injected pigs 5 to 6 cm. long it is plain that a very abundant plexus of lmyphatics from the root of the sac stalk completely surrounds the external jugular vein, and this external jugular plexus has numerous connections with the cervical plexus at its caudal end. The plexus around the external jugular vein empties mainly into the sac stalk, but a single vessel may join the external jugular vein. It must be said in general that the cervical plexus develops from the jugular sac in two places: (1) from the apex of the sac over the sternocleidomastoid muscle, and (2) from the sac stalk along the external jugular vein.

From the cervical plexus there are seven sets of lymphatic capillaries (fig. 16). From the cerebral end of the cervical plexus vessels grow (1) behind the ear, and into a new facial plexus from which vessels grow (2) between the eye and the ear, and (3) over the face. From the ventral border of the cervical plexus there is (4) a set of submaxillary lymphatics which supplies the lower jaw and tongue and (5) superficial lymphatics for the skin of the neck. From the caudal end of the cervical plexus grow (6) the superficial lymphatics of the arm, and (7) the superficial lymphatics of the thorax.

Thus to sum up the superficial lymphatics for the jugular sacs: from the sac stalk and anterior curvature arise the pharyngeal, Eustachian and nasal vessels, from the apex of the sac arise the suprascapular and occipital lymphatics, while from the cervical plexus arise the posterior auricular, temporal, facial, submaxillary, anterior cervical and the superficial lymphatics of the arm and thorax. These groups of lymphatics begin as distinct plexuses of vessels which arise from the sac or from the secondary cervical plexus which in turn comes from the sac. In fig. 8 is shown particularly well how distinct the groups may be at the start. Subsequently all of the groups anastomose and this is an important point.

In fig. 8 it will be seen, for example, that the large vessels of the suprascapular region drain into the apex of the sac, but some of them have small connections with the cervical plexus. In fig. 16 these connections are so much more abundant that they exceed in number those that pass to the sac itself. This point of the anastomoses of the dfficult groups of vessels is well shown in fig. 5 (Sabin 130), where practically all of the superficial lymphatics in the embryo pig 5.5 cm.

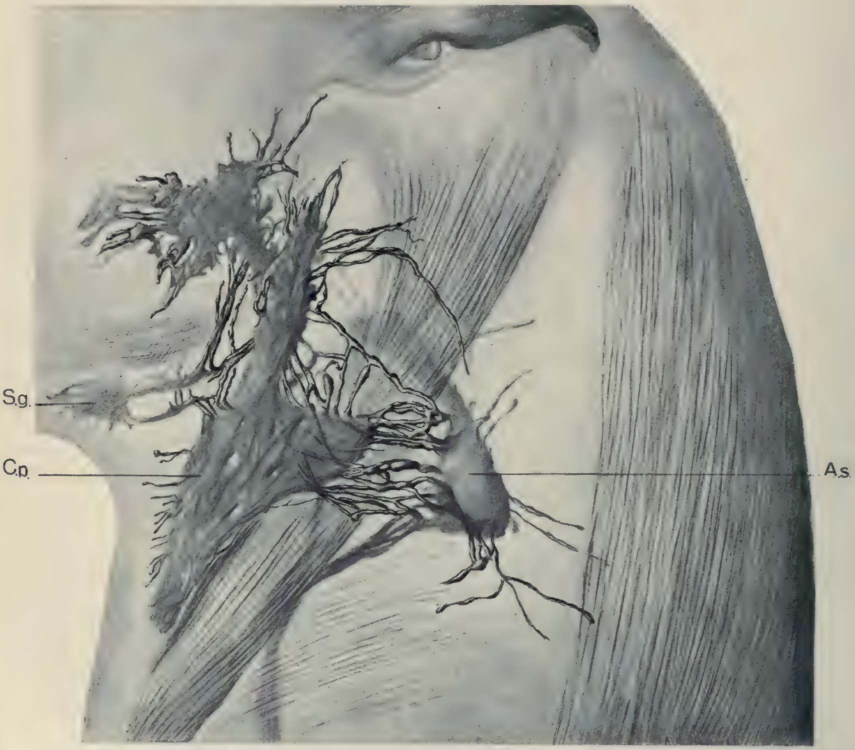

FIG. 17.—Injection of the jugular lymph sac and the cervical lymphatic plexus of a fœtal pig 7.5 cm. long to show the relation of the developing lymph glands to the jugular sac. After A. H. Clark (24). Magnified 5 times. Fixed in 10 per cent formol and cleared by the Spalteholz method. A. s. = apex of the sac, which is now a lymph gland in the posterior triangle of the neck; the anterior curvature of the sac, which is now a deep jugular lymph gland, lies behind the sternocleidomastoid muscle. C. p. = superficial cervical lymphatic plexus, which will become a group of lymph glands. At the cerebral end of the cervical plexus a developing facial lymph gland; S. g. = lympho-glandula submaxillaris.

long have been injected from one puncture. This is a complete injection, which it is clear that fig. 16 is not. In fig. 5 (Sabin 130) for example the lymphatics between the eye and ear are terminal ducts.

Good examples of the anastomoses of different groups of lymphatics are shown in fig. 16 in the vessel which connects the submaxillary and the facial plexus; moreover the thoracic, cervical and brachial plexuses are continuous.

In the embryo pig from 5 to 5.5 cm. long there are no valves in the ducts. It is also the stage of the simple primary plexus of lymphatics. In fig. 16 a secondary plexus of finer lymphatics is growing more superficially and by the time the embryo is from 6 to 7 cm. long there is a deep plexus with valves and a finer-meshed superficial plexus.

The relation of the jugular lymph sacs to lymph glands is shown in fig. 17. Here it is clear that the sac stalk and anterior curvature lie beneath the sternocleidomastoid muscle and that the apex of the sac lies in the posterior triangle of the neck. That the cervical plexus is now a lymph gland is clear, and there is a facial and submaxillary gland also. The cervical plexus becomes a group of glands.

The account of the peripheral lymphatics from the jugular sacs is not complete without mention of the lymphatics of the heart and lungs. These lymphatics have not yet been worked out, but it can be said that there are two sets of lymphatics for the lungs, the deep and the superficial or pleural. The deep lymphatics develop from the jugular sacs; they follow the trachea and are present in a pig measuring 23 mm. and a human embryo measuring 20 mm. I have not injected them and when reconstructed they show the Mayer-Lewis anlagen; that is, in reconstruction they split into a chain of beads. The pleural lymphatics I have injected from the retroperitoneal sac, through the diaphragm to the caudal surface of the lung. Injections of the thoracic duct as, for example, fig. 7 (Nuck 100), also shows vessels from the thoracic duct to the lung. Therefore the lung seems to have a double supply of lymphatics, part from the jugular sac and part from the renal sacs by way of the diaphragm and by way of the thoracic duct.

B. THE PERIPHERAL LYMPHATICS FROM THE RENAL SACS.

The retroperitoneal sacs give rise to the lymphatics of the abdominal viscera except the kidneys. The sac as it lies in the root of the mesentery has been figured by Heuer (43). It spreads over the ventral surface of the Wolffian bodies and supplies their capsule as well as the reproductive glands. From the sac vessels grow to the stomach and the entire intestine, including the rectum. The lymphatics of the diaphragm can be injected from the retroperitoneal sac. The development of the lymphatics of the diaphragm, liver, capsule of the spleen, adrenal and pancreas has not yet been worked out.

Heuer (43) has followed the lymphatics of the intestine from the retroperitoneal sac to the ultimate lacteals. While the embryo is growing from 3 to 4 cm. long a very abundant plexus of capillaries spreads out in the mesentery. The lymphatics reach the wall of the intestine by the time the embryo is 4 cm. long. They first enter the submucosa and form then a primary plexus. Heuer's figures 9 and 10 show that the early vessels in the submucosa have a segmental arrangement, which is, however, nearly lost as the complete plexus forms. The plexus of the mucosa, and of the serosa are both secondary. The lacteals develop from the mucosal plexus and are present in a pig measuring 9 cm. The mesenteric vessels and the submucosal plexus develop valves.

The iliac lymphatics and the thoracic duct: The lymphatics which arise from the mesonephritic veins on the two sides form a very simple pattern. Starting from the veins at the hilus of the two Wolffian bodies they grow caudalward along the edge of the Wolffian bodies to make the iliac sacs, and cerebralward along the dorsal surface of the aorta to form the cisterna chyli. The lymphatics dorsal to the aorta grow in two directions: (1) caudalward to form a chain of prævertebral lymph nodes and (2) cerebralward to form the thoracic duct.

The iliac lymphatic sacs are two long symmetrical sacs extending from the hilus of the Wolffian bodies to the level of the bifurcation of the aorta. In an embryo 23 mm. long they drain into the mesonephritic veins. By the time the embryo is 25 to 27 mm. long this connection is lost and the two iliac sacs converge into the median cisterna chyli dorsal to the aorta.

The caudal end of the iliac lymphatics in the pig is a sac of considerable size, from which three sets of lymphatics can be injected: the ilio-lumbar, the femoral and a plexus which surround the umbilical arteries. The ilio-lumbar superficial lymphatics are very conspicuous in the pig, as shown in figs. 4 and 5 (Sabin 130). This is in marked contrast to the human embryo, where they form part of the inguinal group.

2. Peripheral Lymphatics in Other Forms.

The pattern of the superficial lymphatics in the human embryo is shown in the two figs., 505 and 506 (Sabin 134). This was a remarkable specimen of an embryo 5.5 cm. long which had been kept in formalin some time. On transferring it to freshly made up alcohol, air filled the entire superficial lymphatic system. It shows the primary superficial lymphatic plexus. Valves in a few ducts, namely, the occipital, the thoracic and the inguinal, indicate the oldest vessels. The differences between the superficial pattern in the human and in the pig are mainly the fact that in the human embryo the thoracic lymphatics are much more prominent, draining into the axilla, while in the pig they drain into the superficial cervical plexus, and all the posterior lymphatics drain into the inguinal region in the human embryo. In the human embryo the deep lymphatics for the arm grow from an extension of the jugular sac along the primitive ulnar veins, and the deep lymphatics for the legs grow from the iliac sac along the femoral veins. This shows in fig. 493 (Sabin 134).

Rabbit and cat embryos are like the human in having a marked development of the jugular sac along the primitive ulnar vein (Lewis 76). In this respect they differ from the pig where the axillary lymphatics are smaller. In fig. 7 is shown a deep vessel from the jugular sac, which is, I think, the axillary duct in the pig. In the rabbit and the cat the axillary sac may possibly arise independently of the jugular sac, and in the rabbit a conspicuous chain of peripheral vessels grows along the thoraco-epigastric vein (fig. 8, Lewis 76). Injections of cat embryos show that the axillary lymphatic trunk is very large.

The superficial pattern of the lymphatics in bovine embryos, as shown by Polinski (107), is much like that of the pig.

In the chick the primary lymphatic vessels in the skin connect the posterior lymph heart with the jugular lymph sac along the lateral line in the course of the thoraco-epigastric vein Mierzewski (96) and E. L. Clark (27 and 29).

VI. ORIGIN AND DEVELOPMENT OF LYMPHATIC GLANDS AND THEIR RELATION TO PRIMARY LYMPH SACS.

It is easy to prove that the lymphatic sacs in mammals and the jugular lymph sac in birds become in part lymph glands. I shall define primary lymph glands as those which are derived from the primary lymph sacs.

From the jugular lymph sac in the pig it is clear in fig. 16 that two lymph glands develop: (1) the deep jugular lymph node which drains the pharynx and (2) the node in the posterior triangle of the neck which drains the skin of the anterior part of the body. A. H. Clark (24) has shown that these two glands are single glands in the neck of the adult pig and that they become the largest of all the cervical glands. In the human embryo these two glands are represented by groups of glands, the glands of the posterior triangle and the deep jugular glands. In the human embryo also the group of deep axillary glands comes from an extension of the jugular sac along the primitive ulnar vein and hence they are primary lymph glands. Thus the primary nodes for the anterior part of the body are (1) deep jugular nodes, (2) the nodes of the posterior triangle, (3) the axillary nodes. The relation of the primary lymph gland, both to the various structures of the neck and to the stalk of the jugular sac, that is, to the jugular lymph trunks, is shown especially well in fig. 17 from pig 7.5 cm. long. The anterior curvature and the sac stalk lie behind, that is, medial to the sternocleidomastoid muscle. Of the primary nodes in the neck the deep jugular nodes drain a restricted area, namely, the pharynx and nose; the axillary lymph nodes drain the arm, and the large node of the posterior triangle drains all the rest of the head, face, neck and thorax, either directly or through the superficial cervical plexus. The nodes of the superficial cervical plexus are secondary to the primary lymph sac nodes. It has been brought out that these groups of lymphatics do not remain distinct as they arise, but all become connected with each other through anastomoses of the lymph vessels.

From the retroperitoneal sac develop the retroperitoneal lymph nodes. From the iliac sacs in the pig there is a chain of small nodes lateral to the aorta and a large group of glands on either side opposite the bifurcation of the aorta. These are primary iliac nodes. Dorsal to the aorta is a chain of nodes from the lower end of the cisterna chyli to the bifurcation of the aorta. Thus the renal lymphatics give rise to three groups of primary lymphatic glands: (1) præ-aortic or retroperitoneal, (2) symmetrical iliac nodes lateral to the aorta, and (3) præ-vertebral nodes dorsal to the aorta.

The secondary lymphatic nodes develop along the lymphatic vessels. The most extensive group of secondary nodes in the embryo pig is the one which comes from the superficial cervical plexus along the external jugular vein. In fig. 17 this plexus is shown as one large lymph gland. From the cerebral end of the plexus vessels are forming a gland at the point where the lymphatics divide to form the facial and the temporal lymphatics. The cervical plexus in the adult pig becomes a group of at least a dozen small lymph glands. In both figs. 17 and 18 there is a developing submaxillary lymph gland along the course of the facial branch of the linguo-facial vein (fig. 8). The small facial node and the submaxillary node are tertiary nodes compared with the jugular lymph sac. They show how lymph glands develop at points where lymph ducts radiate out on their development. The primary, secondary and tertiary nodes are constant in the pig.

The mesenteric glands are secondary for the retroperitoneal sac. The secondary glands from the iliac sac are very simple, for there are only two of them: (1) The ileo-inguinal gland, which is very charactesristic of the pig and which remains as a single gland. Its position is readily made out in fig. 4 (Sabin 130), for the superficial lymphatics of the posterior body wall radiate to it. Like the superficial cervical glands it is superficial. (2) The inguinal glands in the pig become a large group of superficial glands, the position of which can be made out in fig. 5 (Sabin 130). The lymph ducts from the inguinal lymph glands develop to the leg, the ventral abdominal wall and the external genital organs. The efferent vessels of the inguinal group of glands and ileo-inguinal gland converge to the large group of primary iliac glands opposite the bifurcation of the aorta.

The histological development of lymph glands is now well understood. The work of Saxer (138) on developing lymph glands considers primarily the development of lymphocytes which I shall not attempt to discuss in this paper, confining the work to the development of the gland as a whole. From the time of Breschet (16) it has been known that lymph glands begin as a plexus of lymphatic ducts. Their development can be followed through the work of Ranvier (117), Bartels (10), Gulland (39), Kling (72), Jolly (59), Lewis (77), and Sabin (131).

The primary lymph glands, which, with the exception of the postaortic, develop out of sacs, begin by a bridging of the sac by bands of connective tissue covered by endothelium. In the case of the retroperitoneal sac these bands are never absent (figs. 498 and 499, Sabin 134). For the jugular lymph sac they show well in human embryo 30 mm. long in fig. 495 (Sabin 134). That these bridges are entirely covered by endothelium is best brought out by total mounts of silver nitrate injections. This has been done for the retroperitoneal sac in the pig. When the primary sacs are thus completely bridged by these bands they are practically a dense plexus of lymphatic capillaries and are therefore in the first stage of the development of lymph glands. At this stage the connective tissue septa are undifferentiated and contain only mesenchyme and blood capillaries.

We are now in a position to consider the question of which are the first lymph nodes in the embryo. This point has been discussed by Lewis (77) and Sabin (131 and 134). It depends on the criterion used. If the criterion is recognizing the formation of a plexus of lymphatic capillaries with undifferentiated connective tissue bridges as the anlagen of a gland, then it is clear that the primary lymph glands, that is, those that come from the lymph sacs, are the first lymph glands to begin for each region of the body. Thus the jugular-subclavian sac in the human embryo is extensively bridged at 30 mm. and is therefore a plexus of lymphatics, the anlage of a lymph gland. At this stage we are agreed there are no lymphocytes (Kling (72), Lewis (77) and Sabin (131)). If, on the other hand, the criterion is the development of the first lymphocytes in the body, we must say that this point has not been reinvestigated since all the primary lymph nodes of the embryo have been determined. Saxer (138, p. 381) notes that lymph nodes are beginning in the neck, the posterior mediastinum, the retroperitoneal tissue, the outside of both hips and along the Wolffian bodies in bovine embryos 4.5 cm. long, and in sheep embryos of the same length describes undoubted wandering cells in the same areas. Kling (72) has no specimens of human embryo between 31 mm., where, he says, there are no lymphocytes in the axillary glands, and 70 m., when lymphocytes are present in many glands. Lewis (77) finds lymphocytes in human embryos 42 mm. long. He finds that they occur practically simultaneously in the glands around the internal jugular vein (primary lymph nodes) and certain "isolated subcutaneous lymph glands," of which he figures one or two along the linguo-facial vein and its branches. The relation of these glands to lymphatic vessels will be readily made out by a comparison of fig. 8 and fig. 16. Figure 8 shows the ducts from the sac along the linguo-facial vein at a stage even younger than Lewis's isolated glands, namely, a pig measuring 3.5 cm. Moreover the beginning cervical plexus from which these submaxillary vessels come shows plainly in fig. 7 from an embryo much smaller, namely, one measuring 18 mm., and they are readily injected in embryos 30 mm. long, fig. 2 (Sabin 130). Thus it is almost certain that the ducts for Lewis's early facial glands in human embryos were present, but could not be found, in sections. It is probable that the lymphocytes begin in human embryos which measure about 40 mm. and they probably develop almost simultaneously in the primary and in the secondary glands.

The plexus stage of developing lymph glands has been shown by reconstruction by Kling (72) and Lewis (77), and by injection in fig. 10 (Sabin 131).

The whole question of the structure of a lymph gland may be summed up in a word by a quotation from Ranvier (p. 1038 in 117): "Un ganglion lymphatique est un angiome caverneux lymphatique qui a été d'abord angiome simple." The development of a gland involves, however, two processes: (1) the formation of lymph sinuses out of lymph plexuses, and (2) the formation of lymph cords and lymph follicles in the trabeculæ. A comparison of Jolly's (59) plates from lymph glands in birds, Kling's (72) figures of human lymph glands, and my own (131) from the developing glands in the pig, will show that the relative proportion of these two parts varies exceedingly in different glands.

The formation of lymph sinuses can be best understood by beginning with Jolly's figures. He shows that in the birds, instead of the mammalian sinus, there is a diffuse plexus of lymphatic vessels with lymphocytes in the septa between the vessels. He also brings out the fact that very large vessels may pass directly through the gland. Thus it is clear that the sinus of birds is a simpler structure than that of mammals. On this account the complete covering of endothelium is very plain in Jolly's figures. Out of a plexus of capillaries such as Jolly shows, the mamalian lymph sinus is formed, as can be seen in fig. 15 (Sabin 131), by an increase in the density of the lymphatic plexus until the septa are reduced to a framework of reticulum covered by endothelium. In this figure all the stages of the formation of a sinus can be seen in a single section. In the lower part of the specimen every lymphatic vessel is plain with its complete lining of endothelium, while in the upper part the septa are in places already reduced to a line. This stage is from an embryo pig 24.5 cm. long, which is the best stage for studying the formation of the sinuses. The question of the development of reticulum has been taken up by Mall (84).

In regard to the formation of the lymph cords and follicles, the fundamental point is the question of the origin of the lymphocytes themselves. This, however, I shall not undertake to discuss. The lymphocytes may occur diffusely in all of the trabeculæ of the developing node and this is the simplest form of a gland. This form is shown by Jolly (59) in his plate IX, fig. 3, for the lumbar glands in birds, by Kling (72), plate XXVII, fig. 11, for the axillary glands in human embryos and in fig. 9 (Sabin 131) from the primary jugular lymph glands in the pig. It will be noted that all of these figures are from primary lymph glands. The definite follicles may develop in the center or in the periphery of a node, and there is every possible variation in the proportion of the diffuse cords and the definite follicles. There are two processes in the development of the follicle: (1) an increase in the number of lymphocytes forming a definite clump, and (2) the formation of a tuft of blood capillaries. Both the cords and the follicles form along the blood vessels, the follicles coming at the capillary bed.

As I have said, the early glands which come from the primary sacs pass through the form of diffuse distribution of the lymphocytes. Follicles which develop later, however, may begin at once as clumps of lymphocytes, making very definite follicles surrounded by a lymphatic plexus. A number of such tiny follicles are to be seen in fig. 16 (Sabin 131), which is the developing group of inguinal lymph glands in a pig 24.5 cm. long.

Lymph glands may be either simple, consisting of one follicle with a peripheral sinus, or compound, with many follicles and cords, and both peripheral and central sinuses.

The subject of hæmolymph glands has been taken up by Helly in the Ergebnisse für Anatomie and Entwickelungsgeschichte for 1902.

VII. COMPARATIVE MORPHOLOGY OF THE PRIMARY LYMPH SACS, LYMPH HEARTS, AMPHIBIAN LYMPH SACS AND LYMPH GLANDS.

We are now in a position to consider the comparative morphology of lymph sacs and lymph hearts. I shall not attempt to analyze the work of Favaro (36a) and of Allen (2-4) on lymphatics in fishes, both of whom state that vessels may function now as veins and now as phatics, but beginning with the amphibia, it is certain that lymphatics bud off from the veins in certain definite areas and form plexuses which are transformed into sacs. The essential structure of these sacs is the endothelial lining. A primary lymph sac is therefore one which buds off from the endothelium of a vein.

In the amphibia, probably in the reptilia, and in the case of the posterior lymph sacs in birds, the primary sacs bud off from segmental veins and rest on the myotomes. They derive striated muscle from the myotomes, which has been shown at least in the case of the anterior lymph hearts in amphibia (Knower 74), and the posterior lymph hearts in reptiles (Stromsen 145) and pulsate rhythmically; in a word, they become lymph hearts.

The lymphatic sacs for the anterior part of the body in birds and all of the lymphatics in mammals do not come from the vertebral and coccygeal veins, but from the anterior cardinal veins in the neck, and the renal veins in the abdomen. These sacs do not lie on the myotomes, they do not receive striated muscle, but rather are transformed into lymph glands. Thus the bird represents a transition stage having a posterior lymph heart and a jugular lymph gland. I shall keep, therefore, the term anterior and posterior lymph hearts, and use the terms jugular and renal lymph sacs. The embryological classification is:

Primary Lymph Sacs.
- 1. Lymph hearts.
  - a. Anterior, amphibia.
  - b. Posterior, amphibia, reptilia and birds.
- 2. Lymph sacs (glands).
  - a. Jugular—birds and mammals.
  - b. Renal
    - Retroperitoneal.
    - Iliac.
    - Cisterna chyli.

The subcutaneous and deep lymph sacs of the amphibia are not primary, but secondary. They are transformed lymphatic ducts. Thus the amphibia have primary lymph sacs which become lymph hearts, lymph ducts which become secondary sacs, and lymphatic capillaries. Mammals have primary lymph sacs which become primary lymph glands, lymphatic ducts which develop valves and along which secondary glands are formed, and thirdly, lymphatic capillaries without valves.

VIII. VARIOUS OTHER THEORIES IN REGARD TO THE ORIGIN AND DEVELOPMENT OF THE LYMPHATIC SYSTEM.

1. Mayer-Lewis Anlagen.

In the preceding pages has been given a consistent account of how the lymphatic system buds off from the veins and gradually invades the body. The places where the lymphatics bud off vary in different forms; in the amphibia and reptiles, and in the case of the posterior lymph hearts in birds the primary lymph sacs lie in the myotomes and receive striated muscle and become lymph hearts. In the higher forms the anterior lymphatics come from the anterior cardinal vein and its branches, the caudal lymphatics do not develop (mammals) and the posterior lymphatics come from the vena cava and renal veins. From these points of origin can be traced all the lymphatics of the body down to the ultimate capillaries.

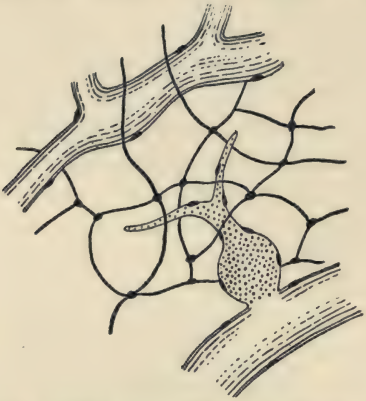

Fig. 18.—Diagram to show the theory of Ranvier and myself that the lymphatics arise from the veins. The veins are striped, the lymphatics dotted.

This theory has not been developed without opposition. In section I it was made clear that the first theory of the origin of the lymphatics was that they arose in the periphery as dilated tissue spaces and grew towards the center, Gulland (39). This was questioned by Sala (137), showing that the first lymphatics in birds were against the veins, and by my proving in 1902 that the jugular lymphatics are the first lymphatics in mammals and that they bud off from the anterior cardinal veins. Thus I substituted for the theories shown in figs. 1, 2 and 3 the simple hypothesis of Ranvier, shown in fig. 18. This indicates that lymphatics bud off as lymphatics from the veins and have the same relation to tissue spaces as have blood capillaries.

The most difficult obstacle in regard to this theory is what we call Mayer-Lewis anlagen. Mayer (89) noted in the tadpole's tail certain isolated vessels which he thought were evidences of the degeneration of blood vessels.

Ranvier (114, p. 578) in studying the plexus of lymphatics of the great omentum in a new-born cat noted that a great many of the vessels terminated in cul de sacs. Some were attached by extremely slender threads, so that they looked as if they were becoming isolated by the atrophy of the intermediate part. Since in the adult cat there are no lymphatics in the omentum, Ranvier interpreted this as a method of degeneration of lymphatic vessels.

The study of the method of degeneration of blood and lymphatic capillaries is an important one. It is obvious that there must be a destruction of capillaries, since a single vessel or a few vessels come from a plexus of capillaries. In Clark's observations (25, p. 191) the usual method of degeneration is by retraction of the processes, but he has also observed (26, p. 410) together with Mayer and Ranvier, that an occasional segment of a blood capillary or lymph capillary may become detached and be left to atrophy. This is in accord with some of the findings of pathology. We must, therefore, conclude that detached, degenerating vessels do occur, though they do not represent the usual method of degeneration.

F. T. Lewis (76) found that in reconstructions lymphatics looked like chains of beads, and to explain this phenomena he suggested that lymphatics might grow by small detached portions of blood vessels. These hypothetical lymphatic anlagen we call Lewis anlagen.

It is clear in watching lymphatics grow, that they never pick up isolated vessels, but grow by the increase in the protoplasm of their own wall; yet it is clear also that reconstructions of uninjected lymphatics appear like rows of beads.

To study this point it was necessary to submit the method of reconstruction to comparative tests with the method of injection and when possible with the method of growth in the living form. This has been done three times (Clark, E. R. 26; Clark, E. L. 27, and Sabin 135).

The best opportunity for studying this point is the tadpole's tail, where, in the living specimen, or in the tail fixed in alcohol, the entire lymphatic system can be seen and drawn. This was done by Clark. The specimen was then cut in serial sections and both blood capillaries and lymphatics were reconstructed. Two reconstructions were made, one with the 4 mm. Zeiss objective, and the other with a 2 mm. Zeiss oil immersion lens. Both reconstructions show that neither blood capillaries nor lymphatic capillaries can be reconstructed completely. More is obtained with an oil immersion lens, but both powers show capillaries in the form of rows of beads (figs. 5, 6 and 7, Clark 26, copied as figs. 513 and 514, Sabin 134).

This test of Clark's is the best possible test, because it is a reconstruction of exactly the same specimen from which the original drawing was made. This point cannot be made in testing the method of injection and that of reconstruction. For this test I (135) used, however, symmetrical plexuses in the same embryo. An embryo pig 27 mm. was chosen in which there was an almost complete injection of the occipital superficial lymphatics. Many of the sprouts on the margin had been ruptured. The injected plexus could of course be reconstructed, while a reconstruction of the empty lymphatics on the opposite side showed the entire plexus split up into isolated vessels (figs. 6, 7 and 8, Sabin 135). On the injected side there was just one lymphatic vessel which did not receive the injection mass, and there was an extravasation just at its base. This is readily explained by the fact that vessels are often connected by very slender strands to the main plexus, as, for example, the vessel near the point of injection in fig. 18, and a rupture might readily occur in such an area before the end of the vessel was reached.

The test of the two methods has now been made a third time by Mrs. E. R. Clark (27) in her injection of the jugular lymphatic plexus in a stage corresponding to the one which Miller (97) has reconstructed. The two results are shown in figs. 14 and 15.

A comparison of the injected jugular sac in a pig 18 mm., shown in fig. 7, with reconstructions of the corresponding stages in the cat (figs. 60 to 62, Huntington 55), also brings out the same point that, wherever the injection method can be applied, it demonstrates more continuous lymphatics in an area than can be reconstructed, even as isolated vessels.

Undoubtedly an occasional blood capillary or lymphatic capillary may separate from the main plexus and atrophy, but the apparently isolated vessels found in serial sections along the course of growing lymphatics connect in life. Lymphatics do not grow by detached blood vessels, and hence the hypothetical Mayer-Lewis anlagen do not exist, that is to say, they are not anlagen of lymphatics, but are parts of a continuous vessel. It is clear that reconstructions of growing lymphatics are valuable, even though they show the lymphatics as rows of beads, provided only the true lymphatics are included; that is to say, the endothelial-lined vessels. For example, Lewis (76, figs. 7 and 8) shows that the early lymphatics in the rabbit grow along the thoraco-epigastric vein.

2. EXTRA-INTIMAL AND PERINEURAL SPACES AND FENESTRATION.

Huntington and McClure (51) began their work on the lymphatic system in 1907 with a study of the jugular lymphatics in the cat. They thought that lymphatics began as clefts between the intima, the vein and the surrounding mesenchyme, so that for a time the wall of a lymphatic was half venous endothelium and half mesenchyme. These spaces they called "extra-intimal" lymphatics. As far as the jugular lymphatic sacs were concerned they subsequently abandoned this idea, accepting the theory that the jugular sacs are derived from the veins (Huntington and McClure 54), but they have since revived the extra-intimal theory in connection with the thoracic duct (Huntington 58).

Their work on the jugular sacs has been given in section IV. In general they accept the theory of the venous origin of the jugular sacs, but they confuse the picture (1) by the inclusion of some perineural spaces (fig. 22, Huntington and McClure 54) and (2) by the idea of fenestration.

The perineural spaces are an interesting phenomenon. I considered them in my first paper in 1902. Along the entire central nervous system and following the peripheral nerves are dilated tissue spaces. Within the spinal canal these spaces are the anlage of the spaces of the pia-arachnoid. Along the nerves we call them perineural spaces. All sections of embryonic tissue show them. They are of undoubted significance for the physiology of the growing nerves, but they never bear any relation to the lymphatics. Injections of them outline the nerves and never enter lymphatic vessels—occasionally they can be injected from the pia-arachnoid, but usually the dense tissue between the vertebræ prevents this.

The question of fenestration was considered in section IV. Parallel veins are formed by the same process of sprouting of endothelium by which all other vessels are formed, and the term fenestration, giving the vague suggestion of the splitting of the wall of a vein once formed, does not describe the actual process and is misleading. We now know that the jugular sacs bud directly from the anterior cardinal vein as lymphatics and grow by the sprouting of their endothelium.

As has been said, Huntington and McClure believe that the jugular lymphatics come from the veins, but that they remain only as a means of communication between the veins and the lymphatic ducts. The lymphatic ducts they think develop in a variety of ways.

The entire question of the method of growth of the lymphatic system is now concentrated on a study of the methods of growth of the thoracic duct. It is probable that the thoracic duct arises in two places; that it is formed in mammals by an asymmetrical downgrowth from the left jugular sac and by a plexus which arises symmetrically from the renal veins and grows along the course of the aorta. This second portion arises later than the first and is in the blood-filled stage (pig 23 mm.) when the jugular stalk is empty. These two anlagen grow as do all other lymphatics and join by the same process by which any lymphatic plexus is formed.

The opposing views are brought out in two papers, one by Huntington (58) and one by Kampmeier (66). Huntington describes a complicated method of origin of the thoracic duct, including (1) a jugular stalk; (2) extra-intimal spaces, and (3) general tissue spaces. Kampmeier, on the other hand, gives a clear and excellent presentation of the theory of the origin of lymphatics by the addition of tissue spaces.

I will begin with the work of Huntington (58). His memoir on the peripheral lymphatics has excellent photographs of sections, so that it is easy to see what he is considering as lymphatics. For example, figs. 1 to 9 are tissue spaces, figs. 10 to 12 are extra-intimal spaces, and figs. 13 to 19 are probably lymphatics. Figure 25 shows the iliac sac labeled 76. Numerous examples of extra-intimal spaces are shown in figs. 105 to 147. Perhaps the best figure of an extra-intimal space is No. 111A. Figures 148 to 158 are lymphatics.

The theory of the origin of lymphatics from extra-intimal spaces has been especially described in an article by Huntington in 1910 (55). In a diagram on page 409 he gives his idea that a space which forms around a degenerating vein eventually includes the entire vein, which then disappears so that the lymphatic is left with a wall of mesenchyme.

There are numerous points which rule out the theory of the origin of the lymphatics by extra-intimal spaces. (1) These spaces can be varied at will by changing the fixation. In my experience they are much more common with lymphatics than with veins. We have sections of adult human tonsils, in which all surrounding lymphatics have extra-intimal spaces. In the human embryo, 460, the large jugular segment of the thoracic duct has one area where the endothelium has sagged from the surrounding tissue. There is, I think, no question but that the extra-intimal spaces are artefacts. This is made the more certain by the fact that they do not occur in the living tadpole's tail, but are found along the veins after fixation.

(2) In connection with the presentation of the extra-intimal spaces, Huntington gives no proof whatever that the structures he figures are degenerating veins. Most of the extra-intimal spaces he shows are along the line of the pulmonary and cardiac lymphatics arising from the jugular sacs. I think it probable from their size and position that the structures he is dealing with are shrunken lymphatics and not veins. The pulmonary and cardiac lymphatics (fig. 13) will, when reconstructed, give the same appearance of isolated lymphatic vessels as all other lymphatic trunks.

(3) The third point against the theory that lymphatics grow by extra-intimal spaces is this: the growing lymphatic tip always keeps as far as possible from the blood capillaries, just as in the adult the ultimate lymphatic capillaries are as far as possible from the blood capillaries; as, for example, in the relation of the central lacteals and peripheral blood capillaries in the villus. The point of the avoidance of the blood capillaries and of the mesenchyme cells as well by the growing lymphatic tip has been well described by Clark (26). Moreover, in certain tadpoles the lymphatics grow out ahead of the blood capillaries where no blood capillaries have ever been. Therefore, lymphatics do not grow by extra-intimal spaces, for extra-intimal spaces are artefacts; there is no evidence that lymphatics follow degenerating veins and on the other hand the growing lymphatic tip, far from following the blood capillaries, avoids them as much as possible.

3. GROWTH OF LYMPHATICS BY THE ADDITION OF TISSUE SPACES.

With these various structures as anlagen of lymphatic capillaries, Huntington and McClure have included certain of the tissue spaces lying along the course of the lymphatics. This theory Huntington brought out especially in a study of the lymphatic system in reptiles (57). After a confused account of the origin of the anterior lymph hearts he describes the development of the peripheral lymph vessels out of tissue spaces. He says that whereas in mammals the greater number of the lymphatic vessels come from extra-intimal spaces (57, p. 272) in reptiles, on the other hand, the lymphatics come from tissue spaces without relation to the veins.

The theory that in the pathway of developing lymphatic vessels certain tissue spaces enlarge and are added onto the growing tips has been worked out by two pupils of McClure, Kampmeier (66a) and Stromsen (146a), both of whom published their work in 1912.

Kampmeier's first article (66) is a preliminary report of the second (66a). He has worked on the development of the thoracic duct in the pig and bases most of his conclusions on a reconstruction of a specimen of mine. Kampmeier thinks that the thoracic duct develops in an anterior-posterior direction by the addition of certain connective tissue spaces which enlarge in the pathway of a developing vessel. This is a return to the view of the earlier embryologists, except that they believed that the growth was from the periphery toward the center.

To a certain extent Kampmeier still holds to the theory of lymphatics from extra-intimal spaces; that is, he believes that a part of the thoracic duct follows veins that are degenerating. A vein which lies in the pathway of a developing lymphatic vessel he calls a "veno-lymphatic." This is a different use of the term from that of Huntington and McClure, who used the term to mean a vein which was transformed into a lymphatic vessel. This latter use of the term can well be given up, since veins do not become lymphatics. The replacing of degenerating veins Kampmeier does not regard as a fundamental process in the development of lymphatics, since they may or may not follow such veins. He thinks that in the development of the thoracic duct about half the duct comes from extra-intimal spaces (66a, p. 434). It is interesting to note in connection with the degeneration of veins in Kampmeier's work that he speaks of the plexus of veins medial to the nervous sympatheticus, fig. 11 (or fig. 11 in 66a), as veno-lymphatics; that is, as veins which disappear as the thoracic duct forms, and yet this same plexus of veins can be readily injected in embryo pigs 27 to 30 mm. long; stages in which the thoracic duct is well formed. It is true that the blood vessels may not show in uninjected specimens, just as the plexus of blood capillaries around the air cells of an adult lung cannot be reconstructed from sections of uninjected specimens. The degeneration of blood vessels can only be followed by means of complete injections of different stages.

Kampmeier finds another example of lymph vessels which grow by the extra-intimal replacement of veins in the region where the thoracic duct empties into the jugular sac. In his fig. 8 from an embryo 20 mm. long he shows vessels in which there is a considerable sagging of the endothelium from the surrounding tissue, making the so-called extra-intimal spaces. Kampmeier's embryo measuring 20 mm. is about the same stage as mine, measuring 23 mm., since mine was measured before fixation, and hence his figure can be compared with fig. 12, in which a lymphatic injection makes it easy to separate veins from lymphatics. As Hoyer says (49b, p. 536): "Den Verlauf der Lymphgefässe nur an nicht injizierten Serienschnitten zu verfolgen, ist eine mühevolle und zeitraubende Arbeit, deren Ergebnisse, wie wir uns selbst überzeugt haben, höchstens nur für grössere Lymphstämme, deren Lage man kennt, als sicher zu bezeichnen sind. Ist der Verlauf von Gefässen und deren Verästelung noch unbekannt, so lassen sich auf Grund von Serienschnitten nur Vermutungen über Verlauf und Verästelung derselben austellen. Erst wenn man über Gefässe und ihre Aeste mit Injektionsmasse gefüllt vor sich sieht, erhält man einen guten Einblick in die Verteilung derselben, deren Verfolgung selbst an nicht injizierten Serienschnitten dann keine wesentlichen Schwierigkeiten mehr bietet." Although it is not possible to be entirely sure in regard to Kampmeier's sections, yet it is at least probable that he is dealing in large part with lymphatics and not with veins at all. The sagging of the endothelium from the surrounding tissue I have found more often with lymphatics than with veins, and yet in tissues fixed in Zeuker's fluid, which Kampmeier uses exclusively, it may occur in any of the veins and even in the aorta. Kampmeier says, with reference to this group of vessels (fig. 8 and fig. 29 in 66a, p. 460), that they are mesenchymal, perivascular spaces into which the jugular sac opens freely; that is, he thinks that the jugular sac in an embryo 20 mm. long opens freely into the tissue spaces. This point is easy to disprove, for in contrast to the early stages of the thoracic duct the jugular sac in this stage is easy to inject. If this were true then every injection of the sac in this stage would show extravasations. This is, however, not so. In fig. 7 is an injection of the sac in an embryo 18 mm. long and I can state with great certainty on the basis of many injections that the jugular sac has a complete endothelial wall and is a closed vessel. It is thus clear that Kampmeier has not demonstrated that this upper part of the thoracic duct replaces degenerating veins.

The chief point, however, in Kampmeier's work is not that some of the lymphatics replace degenerating veins, but that they develop out of tissue spaces. As the chief proof of this theory he uses a reconstruction of an injected specimen of mine. Notwithstanding the fact that this injection is the only one which has yet been made in a mammal in this early stage, Kampmeier does not hesitate to call it complete. It was injected indirectly through the jugular lymph sac, from which the injection mass ran into the thoracic duct. At a certain point in the injection there is an extravasation (Kampmeier, fig. 13, line 15), and in exactly the same position in the next section is a large endothelial-lined empty space. It is therefore merely an arbitrary decision whether the empty vessel was actually connected with the injected part or not, that is to say, there is as much evidence for the one view as for the other. No one who has had experience with the injection method would be sure that the first injection in a new region was a complete one. The spaces which Kampmeier has shown as lymphatics in my specimen are lined by endothelium; that is, they are the spaces with which Lewis (76) has made us familiar; they are not the mesenchyme spaces which Kampmeier and Stromsen regard as the anlage of lymphatics.

Stromsen (146a) has injected the prævertebral lymphatics in turtles and finds that in advance of the injected zone there are enlarged tissue spaces which he thinks are going to become lymphatics. Kampmeier says that it is easy to select tissue spaces which are going to become lymphatics for, "histologically, all incipient lymphatic anlagen, whether they are spaces independent in position or spaces following, transforming and expanding the discarded pathways of redundant venous channels, are decidedly different from either an active vein or a mature lymphatic" (Kampmeier 66a, p. 430). Stromsen (146, p. 354) adds to this ability to select tissue spaces which are going to become lymphatics this further point, that such enlarged tissue space occur only in the pathway of developing lymphatics. These two points can be easily disproved by anyone who has access to serial sections of embryos. For example, why were not the enlarged tissue spaces in Kampmeier fig. 3 selected as lymphatics? Good examples of such spaces are the constantly occurring spaces in the parietal pleura on either side of the vertebra. They are always present in the stages in which the thoracic duct is developing; they are adjacent to the vascular zone just internal to the ribs and they never have any relation to lymphatics. A definite, constant group of such spaces is also to be found in the subcutaneous tissue of the mid-dorsal line of certain stages and they never become lymphatics. The pia-arachnoid and perineural spaces likewise never become lymphatics. In fact, large as well as small groups of such spaces are a constant occurrence in sections of embryos; sometimes near lymphatics and sometimes far from them. The selection of certain tissue spaces as destined to become lymphatics is an arbitrary selection and brings us back to the confused standpoint of the earlier embryologists; a standpoint which would indeed justify the view of Bartels that the question of the relation of the lymphatics to the tissue spaces is "eine philosophische, keine anatomische Frage."

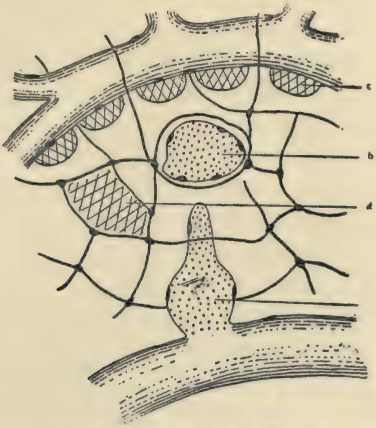

Fig. 19.—Diagram to show some of the various structures which Huntington and McClure have described as lymphatics. a. = true lymphatic capillaries; b. = Mayer-Lewis anlagen, also true lymphatic capillaries; c. = extra-intimal hypothetical lymphatic capillaries; d. = tissue spaces. The perineural spaces are not shown. The veins are striped, lymphatic capillaries dotted, and hypothetical lymphatic capillaries are cross-hatched.

The difficulty of finding out the method of growth by observing sections is best illustrated by following the different theories of their growth in the pages of Huntington and McClure. Some of these methods are shown in the diagram, fig. 19. This development of the subject has been necessarily confusing to those who have not followed the subject carefully. However, now that the origin and method of growth of the lymphatic system has been cleared up, so that the fundamental morphology is understood, the controversy has had this great value, that it has brought up for analysis and discussion every conceivable method of growth. Lymphatics do not arise as dilated peripheral tissue spaces after the manner of the cœlom as the earlier embryologists thought; they do not grow by the addition of hollow connective tissue cells, as Schwann and Virchow thought; they do not rise as perineural spaces, nor by fenestration of a vein, nor by extra-intimal clefts, nor by the progressive addition of connective tissue spaces, nor by the addition of detached blood vessels, but they bud from the veins and grow by the sprouting of their endothelial wall.

IX. CONCLUSIONS.

The most important result of this study on the morphology of the lymphatic system is the emphasis it throws on the importance of endothelium as a tissue. The angioblast is one of the early tissues to be differentiated; it is not an inert lining for vessels, but an actively growing functioning tissue. In its place of growth it is a syncytium of actively amœboid protoplasm. Mollier (99) has shown that in the spleen it may be reticular; Mall (86 and 87) has shown that it may give rise to reticulum. Undoubtedly the further development of our knowledge of endothelium depends on the development of the new experimental anatomy.

The lymphatic endothelium buds off from the veins. It is always a little different in appearance from the endothelium of the veins, and the lymphatic capillary is different in size and form from the blood capillaries. The growing lymphatic tip has the remarkable characteristic that it avoids the blood capillaries, while it is attracted by other lymphatic capillaries.

Endothelium is the essential tissue of the lymphatic system. In the lower vertebrates lymph hearts are formed by the addition of striated muscle to primary lymph sacs. In the higher forms lymph glands are formed by the development of lymphocytes around the ducts. This takes place not only in the wall of the primary lymph sacs, but along plexuses of ducts, so that there are primary and secondary lymph glands.

The fundamental morphology of the lymphatic system has been established, but there remain many gaps in our knowledge of the system as a whole. The deep lymphatics in amphibia and reptilia are almost unknown; in fact a complete account of the lymphatic systems in both of these groups would be of great value. In birds the origin of the iliac lymphatics and the growth of the thoracic duct would be most interesting. In mammals the gaps in our knowledge are especially in regard to the development of the lymphatic system within many of the organs; for example, the heart and lungs, the liver, spleen, kidneys and reproductive organs. A study of the embryology of the lymphatic system makes it more certain that the central nervous system has no lymphatics. The lymphatics invade the body, but not completely; the nervous system is a permanent non-lymphatic area.

It is now possible to define the lymphatics. Lymphatic capillaries are tubes of endothelium; they are derived from the endothelium of the veins, and they have the same relation to tissue spaces as have blood capillaries.

LITERATURE.

1. ABEL, J. J.: On the action of drugs and the function of the anterior lymph hearts in cardiectomized frogs. Journ. of Phar. and Exp. Ther., Vol. 3, 1912.
2. ALLEN, W. F.: Distribution of the lymphatics in the head, and in the dorsal, pectoral, and ventral fine of Scorpænichthys marmoratus. Proc. Wash. Acad. of Science, Vol. 7, 1906.
3. ——— Distribution of the subcutaneous vessels in the tail region of Lepisosteus. Amer. Journ. of Anat., Vol. 8, 1908; Anat. Record, Vol. 2, 1908.
4. ——— Distribution of the lymphatics in the tail region of Scorpænichthys marmoratus. Amer. Journ. of Anat., Vol. 11, 1910-1911.
5. ARNOLD, J.: Experimentelle Untersuchungen ueber die Entwickelung der Blutcapillaren. Arch. für path. Anat., Bd. 53, 1871 and Bd. 54, 1872.
6. ——— Ueber die Beziehung der Blut- und Lymphgefässe zu den Saftkanälen. Arch. für path. Anat., Bd. 63, 1875.
7. v. BAER: Entwickelungsgeschichte der Tiere. I. Teil, 1828. II. Teil, 1837.

8. BAETJER, WALTER A.: On the origin of the mesenteric sac and thoracic duct in the embryo pig. Amer. Journ. of Anat., Vol. 8, 1908.

9. BARAŃSKI, J.: Die Entwicklung der hinteren Lymphherzen der Unke (Bombinator). Bull. de l'Académie des Sciences de Cracovie. Classe des Sciences Mathématiques et Naturelles. Série B. Sciences Naturelles, 1911.

10. BARTELS, P.: Das Lymphgefässystem. Handbuch der Anatomie des Menschen. Von Bardeleben, 1909.

11. BAUM, H.: Können Lymphgefässe direkt in Venen einmünden? Anat. Anz., Bd. 39, 1911.

12. BICHAT: Anatomie Générale, 1818.

13. BOERHAVE: Quoted from Bichat., Anat. Gén., S. 596.

14. BONNET, R.: Grundriss der Entwicklungsgeschichte. Berlin, 1891; Zweite Auflage, 1912.

15. BREMER, H. L.: The development of the aorta and aortic arches in rabbits. Amer. Journ. of Anat., Vol. 13, 1912.

16. BRESCHET, G.: Le Systéme Lymphatique. Paris, 1836.

17. BUDGE, ALBRECHT: Neue Mittheilungen ueber die Lymphgefässe der Leber. Königl. Sachs. Gesellsch. d. Wiss. zu Leipzig. Math.-Phys. Classe. Berichte 27-30, 1875-80, S. 161.

18. ——— Die Lymphwurzeln der Knochen. Arch. f. mik. Anat. 13, 1877.

19. ——— Ueber ein Kanalsystem in Mesoderm von Hühnerembryonen. Arch. für Anat. und Phys., Anat. Abth., 1880.

20. ——— Ueber das dem zweiten Blutkreislaufs entsprechende Lymphgefässystem bei Hühnerembryonen. Centralbl. f. d. med. Wissensch., 1881.

21. ——— Ueber Lymphherzen bei Hühnerembyronen. Arch. für Anat. und Phys., Anat. Abth., 1882.

22. ——— Untersuchungen über die Entwickelung des Lymphsystems beim Hühnerembryo. Arch. für Anat. u. Phys., Anat. Abth., 1887.

23. CRUIKSHANK, W.: The anatomy of the absorbing vessels of the human body. London, 1790.

24. CLARK, A. H.: On the fate of the jugular lymph sacs, and the development of the lymph channels in the neck of the pig. Amer. Journ. of Anat., Vol. 14, 1912.

25. CLARK, E. R.: Observations on living growing lymphatics in the tail of the frog larva. Anat. Record, Vol. 3, 1909.

26. ——— An examination of the methods used in the study of the development of the lymphatic system. Anat. Record, Vol. 5, 1911.

27. Clark, Eleanor Linton: Injection and reconstruction of the jugular lymph sac in the chick. Anat. Record, Vol. 6, 1912.

28. ——— General observations on early superficial lymphatics in chick embryos. Anat. Record, Vol. 6, 1912.

29. Clark, Eliot R., and Eleanor L.: Observations on the development of the earliest lymphatics in the region of the posterior lymph heart in living chick embryos. Anat. Record, Vol. 6, 1912.

30. Clark, Eliot R.: Further observations on living growing lymphatics: their relation to the mesenchyme cells. Amer. Journ. of Anat., Vol. 13, 1912.

31. Drasch, O.: Die Bildung der Somatopleura und der Gefässe beim Hühnchen. Anat. Anz. 9, 1894; S. 567.

32. Dziurzynski, A.: Untersuchungen ueber die Regeneration der Blut und Lymphgefässe im Schwanze von Froschlarven. Bull. de l'Académie des Sciences de Cracovie. Classe des Sciences Mathématiques et Naturelles. Série B. Sciences Naturelles, 1911.

33. Evans, H. M.: On the development of the aorta, cardinal and umbilical veins, and the other blood vessels of vertebrate embryos from capillaries. Anat. Record, Vol. 3, 1909.

34. ——— On the earliest blood vessels in the anterior limb buds of birds and their relation to the primary subclavian artery. Amer. Journ. of Anat., Vol. 9, 1909.

35. ——— Die Entwicklung des Blutgefässystems. Handbuch der Entwicklungsgeschichte des Menschen. Keibel und Mall. Bd. 2. Leipzig, 1911.

36. Favaro, G.: Ricerche anatomo-embriologiche intorno alla circolatione caudale ed ai cuori linfatici posteriori degli Anfibi con particolare riguardo agli Urodeli. Atti del l'Acad. Sc. veneto-trentino-istriana. Cl. 1, 1906.

36a. ——— Ricerche interno all morfologia ed all sviluppo dei vasi, seni e cuori caudali nei Ciclostomi e nei Pesci. Atti del Reale Instituto Veneto di sc. lett. ed arti. Venezia. T. 65, 1906.

37. Goette: Entwickelungsgeschichte der Unke als Grundlage einer vergleichenden Morphologie der Wirbelthiere. Leipzig, 1874.

38. Goldfinger, Gizella: Ueber die Entwickelung der Lymphsäcke in den hinteren Extremitäten des Frosches. Bull. de l'Académie des Sciences de Cracovie. Classe des Sciences Mathématiques et Naturelles, 1907.

39. Gullund: The development of lymphatic glands. Journ. of Path. and Bact., Vol. 11, 1894.

40. Hahn, H.: Experimentelle Studien über die Entstehung des Blutes und der ersten Gefässe beim Hühnchen. Archiv für Entwicklungsmechanik der Organismen. Bd. 27, 1909.

41. Haller: Elementa physiologiæ corporis humani. T. 1. 1757-63, s. 110.

42. Helly, Konrad: Hæmolymphdrüsen. Ergebnisse der Anatomie und Entwickelungsgeschichte. Bd. 12, 1902.

43. Heuer, George J.: The development of the lymphatics in the small intestine of the pig. Amer. Journ. of Anat., Vol. 9, 1909.

44. His, W.: Ueber die Wurzeln der Lymphgefässe in den Häuten des Körpers und über die Theorien der Lymphbildung. Zeitschr. f. wissensch. Zoölogie, XII, 1863.

45. ——— Ueber das Epithel der Lymphgefässwurzeln und ueber die von Recklinghausenschen Saftcanälchen. Zeitsch. f. wissensch. Zoologie, XIII, 1863.

46. ——— Untersuchungen ueber die erste Anlage des Wirbeltierleibes. Leipzig, 1868.

47. ——— Lecithoblast und Angioblast der Wirbeltiere. Abhandl. der mathematisch-physischen Klasse der Königl. Sächs. Gesellsch. d. Wissenschaften. Bd. 26, 1900.

48. Hoyer, H.: Ein Beitrag zur Histologie bindegewebiger Gebilde. Arch. für Anat. und Phys. und wiss. Medicin, 1865.

49. ——— Untersuchungen ueber das Lymphgefässystem der Froschlarven. Bull. de l'Académie des Sciences de Cracovie. Classe des Sciences Mathématiques et Naturelles, 1908.

49a. ——— Zur Entwicklung der Lymphgefässe bei Wirbeltieren. Verhandl. d. VIII Internat. Zool. Kongr. zu. Graz. (vom. 15-20, 8, 1910), 1912.

49b. ——— Und Udziela, S., Untersuchungen ueber das Lymphgefässystem von Salamanderlarven. Morph. Jahrb., Bd. 44, 1912.

50. Hunter, W.: Medical Commentaries. Deutsch. von. Kühne als medicinisch-chirurgische Beobachtungen. Leipzig, 1785. Bd. 2.

51. Huntington, G. S., and McClure, C. F. W.: The development of the main lymph channels of the cat in their relations to the venous system. Anat. Record, Vol. 1, 1906-1908.

52. ——— The anatomy and development of the jugular lymph sacs in the domestic cat. Anat. Record, Vol. 2, 1908.

53. Huntington, G. S.: The genetic interpretation of the development of the mammalian lymphatic system. Anat. Record, Vol. 2, 1908.

54. Huntington, G. S., and McClure, C. F. W.: The anatomy and development of the jugular lymph sacs in the domestic cat. Amer. Journ. of Anat., Vol. 10, 1910.

55. Huntington, G. S.: The phylogenetic relations of the lymphatic and blood vascular system in vertebrates, p. 1, and The genetic principles of the development of the systemic lymphatic vessels in the mammalian embryo, p. 339. Anat. Record, Vol. 4, 1910.

56. ——— Ueber die Histogenese des lymphatischen Systems beim Säugerembryo. Verhandl. der Anat. Gesellsch., 1910.

57. ——— The development of the lymphatic system in reptiles. Anat. Record, Vol. 5, 1911.

58. ——— The anatomy and development of the systemic lymphatic vessels in the domestic cat. Memoires of the Wistar Institute of Anatomy and Biology, No. 1, 1911.

59. Jolly, J.: Recherches sur les ganglions lymphatiques des oiseaux. Arch d'Anat. microsc., T. 11, 1910.

60. Jourdain, M. S.: Sur l'existence d'une circulation lymphatique chez les Pleurometes. Comptes Rendus de l'Académie des Sciences, 90, 1880, p. 1430.

61. Jourdain, M. L.: Sur le systéme lymphatique des têtards et grenouilles. Comptes Rendus de l'Académie des Sciences, 96, 1883.

62. Jossifrow, G.: Zur Lehre von dem Lymphgefässystem der Froschlarve, des Frosches und der Eidechse. Ref. in Schwalbe's Jahresber., 1905, III, S. 353.

63. Jossifrow, S. M.: Ueber die Bedeutung des Cisterna chyli für die Lymphbewegung. Russki Wratsch. Jahrg. II. N. 29, S. 1909-1910.

64. Jossivow, G.: Sur le systéme lymphatique du têtard, de la grenouille et du lézard. 1 Taf. Mém. l'Acad. Imp. des Sc. St. Petersbourg. Sér. 8. T. 15. N. 11, p. 20.

65. ——— Der Anfang des Ductus thoracicus und seine Erweiterung. Trav. Soc. Méd. scientif. et. hyg. Charkoff. S. 1-9.

66. Kampmeier, O. F.: The value of the injection method in the study of lymphatic development. Anat. Record, Vol. 6, 1912.

66a. ——— The development of the thoracic duct in the pig. Amer. Journ. of Anat., Vol. 13, 1912.

67. Koelliker: Sur le developpement des tissues chez les batraciens. Annales des Sciences Naturelles, IIIe Serie, 1846.

68. ——— Ueber die Blutkörperchen eines menschlichen Embryo und die Entwicklung der Blutkörperchen bei Säugetieren. Zeitschrift f. rationelle Medizin. Henle und Pfeufer. Bd. IV, 1846.

69. ——— Entwicklungsgeschichte des Menschen und der höheren Tiere. Zweite Auflage. Leipzig 1876, S. 158.

70. ——— Grundriss der Entwickelungsgeschichte des Menschen und der höheren Tiere. 2 Aufl. Leipzig 1884.

71. ——— Histologische Studien an Batrachierlarven. Zeitschr. f. wissensch, Zoologie. 43, 1886.

72. Kling: Studien über die Entwickelung der Lymphdrüsen beim Menschen. Upsala Läkareförenings Föranslinger. 1903, and Arch. f. mikr. Anat. u. Entwicklungsgesch. Bd. 63, 1902.

73. Knower, H. McE.: Effects of early removal of the heart and arrest of circulation on the development of frog embryos. Anat. Record, Vol. 1, 1907.

74. ——— The origin and development of the anterior lymph hearts and the subcutaneous lymph sacs in the frog. Anat. Record, Vol. 2, 1908.

75. Langer, C.: Ueber das Lymphgefässystem des Frosches. Die Lymphgefässe im Schwanze der Batrachierlarven. Sitzungsber. d. k. Akad. d. Wissensch. Bd. 58, 1868.

76. Lewis, F. T.: The development of the lymphatic system in rabbits. Amer. Journ. of Anat., Vol. 5, 1906.

77. ——— The first lymph glands in rabbit and human embryos. Anat. Record, Vol. 3, 1909.

78. ——— On the cervical veins and lymphatics in four human embryos, with an interpretation of anomalies of the subclavian and jugular veins in the adult. Amer. Journ. of Anat., Vol. 9, 1909.

79. MacCallum, W. G.: Die Beziehung der Lymphgefässe zum Bindgewebe. Arch. für Anat. und Phys., Anat. Abth., 1902.

80. Mall, F. P.: Development of the ventral abdominal walls in man. Journ. of Morphology, Vol. 14, No. 2, 1898.

81. ——— The cœlom. Reference Handbook of the Medical Sciences. William Wood & Co., New York. Second Edition. 1900-1904.

82. ——— Development of the internal mammary and deep epigastric arteries in man. John Hopkins Hospital Bulletin, 1898.

83. ——— On the origin of the lymphatics in the liver. Proceedings of the Association of American Anatomists, 1900.

84. ——— Development of the connective tissues from the connective syncytium. Amer. Journ. of Anat., Vol. 1, 1901-1902, p. 354.

85. ——— On the development of the blood vessels of the brain in the human embryo. Amer. Journ. of Anat., Vol. 4, 1905.

86. ——— A study of the structural unit of the liver. Amer. Journ. of Anat., Vol. 5, 1906.

87. ——— On the development of the human heart. Amer. Journ. of Anat., Vol. 13, 1912, p. 258.

87a. Marcus, H.: Beiträge zur Kenntniss der Gymnophionen. Morphologisches Jahrb. Bd. 38, 1908.

88. Mayer, J.: Ueber die Neubildung von Blutgefässen in plastischen Exsudaten seröser Membranen und in Hautwunden. Annal. d. Charité, IV, p. 41-140.

89. Mayer, Sigmund: Ueber die blutleeren Gefässe im Schwanze der Batrachierlarven. Sitzungsberichte, der math. naturwissenschaftlichen Classe der Kaiserlichen Akademie der Wissenschaften in Wien. Bd. 91, III Abth., 1885, S. 204.

89a. Meyer, F.: Systema amphibiorum lymphaticum disquisitionibus novis examinatio. Diss. inaug, Berolini, 1845. Quoted from Hoyer (49b).

90. Maximow, A.: Untersuchungen ueber Blut und Bindegewebe. Archiv für mikroskopische Anatomie und Entwickelungsgeschichte, Bd. 73, 1909.

91. McClure, C. F. W.: The development of the thoracic and right lymphatic ducts in the domestic cat (Felis domestica). Anat. Anz., Bd. 32, 1908.

92. McClure, C. F. W., and Silvester, C. F.: A comparative study of the lymphatico-venous systems in adult mammals. Anat. Record, Vol. 3, 1909.

93. McClure, C. F. W.: The extra-intimal theory and the development of the mesenteric lymphatics in the domestic cat (Felis domestica). Verhandl. der Anat. Gesellsch., 1910.

94. ——— A few remarks relative to Mr. Kampmeier's paper on the value of the injection method in the study of lymphatic development. Anat. Record, Vol. 6, 1912.

95. Meltzer, S. J.: The distribution of solutions in cardiectomized frogs. Journ. of Exper. Med., Vol. 13, 1911.

96. Mierzejewski, Ladislas: Beitrag zur Entwicklung des Lymphgefässystems der Vögel. Bull. de l'Acad. des Sciences de Cracovie. Classe des sciences mathematiques et naturelles, 1909.

97. Miller, A. M.: The development of the jugular lymph sac in birds. Amer. Journ. of Anat., Vol. 12, 1912.

97a. ——— Histogenesis and morphogenesis of the thoracic duct in the chick; development of blood cells and their passage to the blood stream via the thoracic duct. Amer. Journ. of Anat., Vol. 15, 1913.

98. Minot: Die Entwicklung des Blutes. Handbuch der Entwicklungsgeschichte des Menschen. Keibel und Mall. Bd. II, Leipzig 1911.

99. Mollier, S.: Ueber den Bau der kapillaren Milzvenen (Milzsinus). Arch. f. mikr. Anat., Bd. 76, 1911.

100. Nuck, A.: Adenographia curiosa. Leidæ, 1691.

101. Pander: Beiträge zur Entwickelungsgeschichte des Hühnchens im Ei. Würzburg, 1817.

102. Pannizza, B.: Osservazionni antropo-zootomico fissiologiche. Pavia, 1830.

103. ——— Sopra il sistema linfatico dei rettili, ricerche zootomiche. Pavia, 1833.

104. Pensa, A.: Della struttura e dello sviluppo dei gangli linfatici degli uccelli (Ancer domesticus). Ric. f. n. Lab. di Anat. norm. d. R. Univ. di Roma. Vol. 12, 1906-07. Tav. 15. Fig. 2.

105. ——— Studio sulla morfologia e sulla topografia della cisterna chili e del ductus thoracicus nell'uomo ed in altri mammiferi. Ric. f. n. Lab. di Anat. norm. d. R. Univ. di Roma. Vol. 14, 1908-09. Tav. 2.

106. Platner, E. A.: Einige Beobachtungen ueber die Bildung der Capillargefässe. Müller's Archiv f. Anat. Phys. und wissensch. Medicin, 1844, S. 525-526.

107. Polinski, W.: Untersuchungen ueber die Entwicklung der subcutanen Lymphgefässe der Säuger, in sonderheit des Rindes. Bull. de l'Acad. des Sciences de Cracovie. Classe des Sciences Math. et Naturelles, Serie B, 1910.

108. Prévost et Lebert: Mémoire sur la formation des organes de la circulation et du sang dans les batraciens. Ann. des sciences nat. 3 Serie, 1844. T. I, II et III.

109. Radwanska, M.: Die vorderen Lymphherzen der Frösche. Bull. intern. Ac. Sc. Cracovie, 1906.

110. Ranvier, L.: Morphologie du systéme lymphatique. De l'origine des lymphatiques dans la peau de la grenouille. C. R. Ac. des sc. T. 120, 1895, p. 132.

111. ——— Structure des ganglions lymphatiques du porc. C. R. Ac. des sc. T. 121, 1895, p. 800.

112. ——— Étude morphologique des capillaires lymphatiques des mammifères. C. R. Ac. des sc. T. 121, 1895, p. 856.

113. ——— Développement des vaisseaux lymphatiques. C. R. Ac. des sc. T. 121, 1895, p. 1105.

114. ——— Aberration et régression des lymphatiques en voie de développement. C. R. Ac. des sc. T. 122, 1896, p. 578.

115. ——— Des lymphatiques de la villosité intestinale chez la rat et le lapin. C. R. Ac. des sc. T. 123, 1896, p. 923.

116. ——— La théorie de la confluence des lymphatiques et la forphologie du système lymphatique de la grenouille. C. R. Ac. des sc. T. 123, 1896, p. 970.

117. ——— La théorie de la confluence des lymphatiques et la développement des ganglions lymphatiques. C. R. Ac. des sc. T. 123, 1896, p. 1038.

118. ——— Morphologie et développement des vaisseaux lymphatiques chez les mammifères. Archives d'Anatomie microscopique. T. 1, 1897, p. 69 et p. 137.

119. Von Recklinghausen: Die Lymphgefässe und ihre Beziehung zum Bindegewebe. Berlin, 1862.

120. ——— Das Lymphsystem. Stricker's Handbuch der Lehre von den Geweben. Leipzig, 1871-72.

121. Reichert, K. B.: Studien des physiologischen Instituts zu Breslau. Leipzig, 1858.

122. ——— Entwicklungsleben im Wirbelthierreich. Berlin, 1840 und 1857.

123. ——— Entwicklung des Meerschweinchens. Abh. der Berliner Akad., 1862.

124. Remak, R.: Untersuchungen ueber die Entwickelung der Wirbeltiere. Berlin, 1850-55.

125. ——— Ueber blutleere Gefässe (Lymphgefässe) im Schwanze der Froschlarve. Müller's Archiv f. Anat. Phys. und wiss. Medicin. 1850. S. 102 und S. 182.

126. Rouget, Charles: Mémoire sur les développement, la structure et les propriétés physiologiques des capillaires sanguins et lymphatiques. Arch de Phys., V, 1873.

127. Rückert: Ueber die Abstammung der blutigen Gefässanlagen beim Huhn, und ueber die Entstehung des Randsinus beim Huhn und bei Torpedo. Sitzungsber. d. k. bayer. Akad. d. Wissensch. zu München, 1902.

128. Rückert, J.; und Mollier, S.: Die erste Entstehung der Gefässe und des Blutes bei Wirbeltieren. Handbuch der vergleichenden und experimentellen Entwickelungslehre der Wirbeltiere. Hertwig, Bd. I. T. 1, 1906.

129. Sabin, F. R.: On the origin of the lymphatic system from the veins and the development of the lymph hearts and thoracic duct in the pig. Amer. Journ. of Anat., Vol. 1, 1901-02.

130. ——— On the development of the superficial lymphatics in the skin of the pig. Amer. Journ. of Anat., Vol. 3, 1904.

131. ——— The development of the lymphatic nodes in the pig and their relation to the lymph hearts. Amer. Journ. of Anat., Vol. 4, 1905.

132. ——— Further evidence on the origin of the lymphatic endothelium of the blood vascular system. Anat. Record, Vol. 2, 1908.

133. ——— The lymphatic system in human embryo, with a consideration of the morphology of the system as a whole. Amer. Journ. of Anat., Vol. 9, 1909.

134. ——— Die Entwicklung des Lymphgefässystems. Handbuch der Entwicklungsgeschichte des Menschen. Keibel und Mall, Vol. 2, Leipzig, 1911. Manual of Human Embryology, Keibel und Mall. J. B. Lippincott Co., 1912.

135. ——— A critical study of the evidence presented in several recent articles on the development of the lymphatic system. Anat. Record, Vol. V, 1911.

136. ——— On the origin of the abdominal lymphatics in mammals from the vena cava and the renal veins. Anat. Record, Vol. 6, 1912.

136a. ——— Der Ursprung und die Entwickelung des Lympfgefässystems. Ergebnisse der Anatomie und Entwickelungsgeschichte, 1913.

137. Sala, L.: Sullo sviluppo dei cuori limfatici e dei dotti toracici nell' embrione di pollo. Ricerche Lab. di Anat. Norm. d. r. Univ. di Roma. Vol. 7, 1899-1900.

138. Saxer, Fr.: Ueber die Entwickelung und den Bau der normalen Lymphdrüsen und die Entstehung der roten und weissen Blutkörperchen. Anat. Hefte. Bd. 6, 1896.

139. Schwann: Structur und Wachstum der Thiere und Pflanzen. Berlin, 1839.

140. Silvester, Charles F.: On the presence of permanent communications between the lymphatic and venous systems at the level of the renal veins in adult South American monkeys. Amer. Journ. of Anat., Vol. 12, 1912.

141. Smith, Helen W.: On the development of the superficial veins in the body wall in the pig. Amer. Journ. of Anat., Vol. 9, 1909.

142. Stannius: Ueber Lymphherzen der Vögel. Müller's Archiv für Anat., Phys. und wiss. Medicin, 1843.

143. Stricker, S.: Studien ueber den Bau und das Leben der capillaren Blutgefässe. Sitzungsbericht der Math.-Naturwiss. Klasse der k. Akad., Wien. Bd. 52. Abth. 2, 1865, S. 379.

144. ——— Untersuchungen ueber die Kontractilität der Kapillaren. Med. Jahrb., Wien, 1878.

145. Stromsen, F. A.: A contribution to the anatomy and development of the posterior lymphatic heart of turtles. Publication 132 of the Carnegie Institution of Washington, 1910.
146. ——— On the relations between the mesenchymal spaces and the development of the posterior lymph hearts of turtles. Anat. Record, Vol. 5, 1911.
146a. ——— On the development of the prevertebral (thoracic) duct in turtles as indicated by a study of injected and uninjected embryos. Anat. Record, Vol. 6, 1912.
147. Szily, A.: Ueber das Entstehen eines fibrillären Stützgewebes im Embryo und dessen Verhältniss zum Glaskörperfrage. Anat. Hefte. Bd. 35, 1908.
148. Thoma: Untersuchungen ueber die Histogenese und Histomechanik des Gefässystems. Stutgart, 1893.
149. Tilney, F.: The development of the veins and lymphatics in Tragulus meminna, erxleben. Amer. Journ. of Anat., Vol. 13, 1912.
150. Virchow: Die Cellularpathologie. Berlin, 1858.
151. Wieliky, W.: Einige Beiträge zur Anatomie und Physiologie der Lymphherzen. Ref. in Hoffmann-Schwalbe's Jahresber., 1884.
152. ———Ueber die Anwesenheit vielzähliger Lymphherzen bei den Froschlarven. Zool. Anz. Bd. 9, 1886.
153. ——— Weitere Untersuchungen ueber die Lymphherzen und Lymphgefässe einiger Amphibien. Ref. in Hoffmann-Schwalbe's Jahresb., 1889.
154. Wolff: Theoria Generationes (Original 1759). Ausgabe von 1764.
155. Wysotzky, N. Th.: Materialien zur embryonalen Entwicklungsgeschichte der Gefässe. Journ. f. norm. u. path. Histologie u. klin. Medicin. Herausgegeben von M. Rudneff. St. Petersburg, 1875. Schwalbe und Hoffmann, Jahresberichte. 1876. S. 145.

THE NUCLEI TUBERIS LATERALES AND THE SO-CALLED GANGLION OPTICUM BASALE.

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There is perhaps no region of the mammalian brain concerning whose cell groups less is known than that portion of the telencephalon known as the pars optica hypothalami. The cell groups which constitute the subject of this article are so vague and so hopelessly confused in the literature that it is not even possible to determine whether the names basal optic ganglion and nuclei tuberis should be applied to different cell groups or to different portions of the same cell group. In this article it will be shown that these names should be applied to entirely different cell groups; moreover the location and extent of the two cell groups will be described in different mammals, together with a consideration of their relation to surrounding groups of cells, and it will be shown that these two cell groups under consideration are composed of cells of radically different character through which each group may be readily distinguished from the other and from the surrounding cell groups. In addition the cell groups of the pars mammillaris of the hypothalamus will be described.

When we consider the methods employed by most of those who study the anatomy of the mammalian brain perhaps it will not be surprising to realize that the best description of the basal optic ganglion and the nuclei tuberis is that of Kölliker published in 1896, however faulty and confusing this description may be. The reason for this lack of information concerning these cell groups is that most workers are interested in the course of fiber tracts, and their interest in the structure of the nervous system is for the most part limited to the largely mechanical subdivisions revealed by fiber stains; in such preparations the course of fiber systems may often be followed, or at least they reveal certain architectural differences of various regions which serve the purpose of orientation. When preparations in which the cells are stained are studied these preparations are for the most part regarded as showing merely the negative picture of the fiber preparations, and the same topographical regions are observed, the cells being stained instead of the fibers. When the cell character is noted it is done usually in a superficial manner and principally for the purpose of orientation, and with no purpose of bringing the cell character into relation with a definite function.

The same lack of attention to the cell type is apparent even in the work of the relatively few investigators who employ the experimental methods of Nissl or von Gudden. The following instance is a good illustration of the value of carefully noting the cell character of various cell groups. In his excellent study of the dorsal (sympathetic) nucleus of the vagus nerve Molhant had shown that all the cells of this cell column give origin to all of the vagus fibers which supply smooth muscle and heart muscle, and that certain portions of this cell column supply smooth muscle while a definite portion supplies heart muscle, but he did not attempt to show that a definite type of cell was involved in the innervation of each of these two types of muscle; after studying the vagus sympathetic nucleus I was able to show that the portions of the nucleus which supply smooth muscle and heart muscle may be readily distinguished by the fact that they are composed of cells of different types, and that just as heart muscle is histologically intermediate between smooth muscle and striated muscle, just so the cells of the vagus sympathetic nucleus which supply heart muscle are of a histological character intermediate between that of the cells which supply smooth muscle and striated muscle. Such an observation of the relation of cell type to cell function enables us to locate accurately a functional center even though its cells be mixed with those having a different function, and homologous centers may be recognized in different animal forms; at the same time it emphasizes the necessity of carefully noting the cell character of each cell group, so that even if the function is unknown the presence of a definite cell type will offer a problem for future experimental work, and in the meanwhile preclude the possibility of confusing this cell group with surrounding cells. These differences in cell type are of course most definite in the higher mammals and especially in man, where the various cell groups are highly specialized.

The foregoing consideration of the failure of workers on the anatomy of the mammalian brain to attach sufficient importance to the different types of cells explains why such characteristic cell groups as the basal optic ganglion and the nuclei tuberis have not been clearly separated from one another and from the surrounding cell groups. The unfortunate condition which here exists is present also in many other regions of the nervous system, and I have considered the tendency of the anatomical work on the mammalian brain somewhat at length not merely as an interesting explanation for our present want of definite information, but because this tendency contains a serious defect whose results are most evident and far reaching, a defect which should be corrected.

The tendency of neurological workers to attach little importance to differences in cell character I have criticised, not only at this point but also later in this article. On the other hand I have no intention whatever of disparaging the ability of other authors, nor am I unappreciative of the excellence, in many cases, of their work and of the valuable results which they have contributed. My criticism is aimed exclusively at the almost universal belief that the various differences in cell type in the nervous system are, after all, of no great importance, and that we should reserve our efforts to discover the connections of various portions of the nervous system. It would be unfair to blame authors for being influenced by a belief so general; moreover it is only comparatively recently that we have begun to employ methods capable of revealing the striking differences in cell character, and only in recent years has the development of cytology given an added stimulus to the careful study of the nerve cell. Above all I wish to disclaim any belief that the method herein employed—that of setting aside groups of cells of an identical type and of comparing such cell groups and of attempting to discover the correlation between cell type and cell function—is of any more value than many other methods of investigation. I advocate it not to displace other methods, but to complement them and add to their usefulness.

MATERIAL.

The material studied consists of the following complete series: four of man, one of macacus rhesus, two of lemur rufus, and three of the cat. The tissue was in each case fixed in 95 per cent alcohol, and after dehydration and treatment with chloroform embedded in paraffin. The sections were stained in a one per cent aqueous solution of toluidin blue (Grübler), differentiated in 95 per cent alcohol, dehydrated in absolute alcohol, cleared in xylol, and mounted in Canada balsam.

Pars Mammillaris Hypothalami.

Before proceeding to describe the cell groups of the pars optica hypothalami (telencephalon) it will be necessary to consider those of the pars mammillaris hypothalami (diencephalon), since the cell groups of these two subdivisions of the hypothalamus are most intimately related and cannot be intelligently studied separately. In 1910 appeared my monograph "Über die Kerne des menschlichen Diencephalon" in which the cell groups of the pars mammillaris hypothalami of man were described, together with a brief consideration of certain closely related cell groups of the pars optica. Since the publication of this monograph I have studied both portions of the hypothalamus in the monkey, lemur and cat, and have compared the cell groups observed in these animals with homologous groups found in man. The following description of the cell groups of the pars mammillaris of the monkey, lemur and cat is accordingly original and I should like to call especial attention to the illustrations which clearly show for the first time the different cell groups in macacus rhesus (Figs. 19 to 25). In Series D of man these cell groups are also well shown (Figs. 11 to 18). The other series do not show much of the pars mammillaris, since it did not appear advisable to add many illustrations to show exclusively portions of the pars mammillaris which are not intimately related to the pars optica. In the series of macacus and the Series D of man the plane of section is such as to include this caudal portion of the pars mammillaris. Moreover the dorsal portion of the pars mammillaris has not been illustrated, not only because it has no close relation to the pars optica but also because the thalamus of the three lower forms must first be studied. Certain types of cells also which on account of their location could not be confused with the cells of the pars optica have not been illustrated. Accordingly it appears best to defer such numerous and elaborate illustrations until the whole diencephalon can be included, and to limit the illustrations of the present article to those portions of the pars mammillaris which are closely related to the pars optica.

In studying the anatomy of the cell groups of the diencephalon nowhere are more satisfactory results obtained than in the hypothalamus (pars mammillaris). The great difficulties encountered in attempting to homologize the cell groups of the thalamus of different mammals disappears when we reach the hypothalamus. This is due to the fact that the thalamus is phylogenetically a much more recent portion of the brain and its development is largely dependent upon that of the rapidly developing pallium. So small is the difference in the cell groups of the hypothalamus of the various mammals studied that for the purposes of this article one description will suffice for all. The pars mammillaris hypothalami is divided into the following primary nuclei (groups of cells having an identical histological character):

1. Ganglion mediale corporis mammillaris.
2. Nucleus intercalatus corporis mammillaris.
3. Nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
4. Nucleus paraventricularis hypothalami.
5. Corpus hypothalamicum (Luysii).
6. Substantia reticularis hypothalami.
7. Substantia grisea ventriculi tertii.

At this point it is advisable to read the explanation of the various kinds of illustrations as given on pp. 39-40; otherwise the figures, some of which are immediately to be referred to, might not be correctly interpreted.

1. *Ganglion mediale corporis mammillaris.*

This cell group constitutes the greater portion of the mammillary body, and extends further caudally than the other two groups. It is shown in the series of macacus (Figs. 19 and 20) and in the Series D of man (Fig. 11); no description of its relations will be given. Concerning its cells it will suffice to state that they are of a type readily distinguishable from the other two groups of the corpus mammillare.

2. *Nucleus intercalatus corporis mammillaris.*

This is a small circumscribed cell group, described by me in 1910, which lies between the medial and so-called lateral ganglion of the mammillary body. Its location may be seen in the same figures that show the medial ganglion (see above). Later Friedemann found this group in cercopithecus and adopted the name here employed. The cells of the nucleus intercalatus are readily distinguished from those of the two other groups of the mammillary body through their characteristic type; especially in man they have the relatively large and discrete Nissl granules characteristic of efferent nerve cells. This cell group should not be confused with groups which are occasionally mechanically split off from the medial ganglion by fiber masses; the difference in cell type renders this distinction easy.

3. *Nucleus tubero-mammillaris.*

The cells of the so-called lateral ganglion of the corpus mammillare may be readily followed orally and laterally into the angle between the pes pedunculi and the tractus opticus, whereas orally and dorsally they may be followed through many sections accompanying the tractus thalamo-mammillaris and the columna fornicis. To this complex of cells having an identical histological character I gave (1910) the name "nucleus mammillo-infundibularis," a name which Friedemann (1911) has adopted in his article on the diencephalon of cercopithecus. It is evident that this name is unsuitable, since the cell group is not situated in the infundibulum, and I have therefore changed it to "nucleus tubero-mammillaris." The nucleus tubero-mammillaris is shown in all the series illustrated and its relation to the basal optic ganglion and the nuclei tuberis may be readily seen. (Since the figures were drawn and labeled before I decided to change the name of this nucleus, it appears on the outline drawings as "nucleus mammillo-infundibularis," but wherever space has permitted the new name has been added in parentheses. The explanation of each plate is so arranged as to remove any possibility of confusion.) The character of its cells in the different forms is illustrated in Figs. 41, 47, 52 and 57. The relation of this nucleus to the basal optic ganglion will be discussed later. It should be noted that a portion of this nucleus is situated in the pars optica.

4. *Nucleus paraventricularis hypothalami.*

This characteristic column of cells is situated partly in the pars mammillaris but principally in the pars optica. Its location is shown in all the series, and the character of its cells in Figs. 43, 49, 54 and 58. In man this nucleus was first described by me in 1910, and the fact that such a striking cell group had not been previously described in man is probably due to the almost exclusive use of fiber stains. In 1911 Friedemann found this cell group in cercopithecus. It is certainly homologous with the group described by Cajal in rodents under the name of "núcleo subventricular," and with that described by Ziehen in marsupials as "Nucleus subcommissuralis." Homologous groups are also possibly found in vertebrates even as low as the fishes. The nucleus paraventricularis is intimately related to the basal optic ganglion and also to the nucleus tubero-mammillaris as these three nuclei appear to be components of one large cell complex, and while differing from one another, differ much more from the surrounding cells. These relations will be discussed later in detail.

5. *Corpus hypothalamicum (Luysii)*

This is such a compact, isolated cell mass, and is situated at such a distance from the basal optic ganglion and the nuclei tuberis that no description is necessary; it has been included in the illustrations, however, for the purpose of orientation.

6. *Substantia reticularis hypothalami.*

This group of cells on account of its position need not be considered in this article. A description will be found in my monograph on the diencephalon. Many of its cells are of a motor type of structure, and these together with the cells of the nucleus intercalatus of the corpus mammillare are the only cells of the entire diencephalon which show the histological character peculiar to motor cells.

7. *Substantia grisea ventriculi tertii.*

This cell mass is shown in all series and the cell type in Figs. 40, 46, 51 and 56. The greater portion lies in the pars optica, and it should be noted that dorsally and laterally the cells are less densely packed than ventrally and medially. The substantia grisea is closely related to the nuclei tuberis, and this relation will be fully discussed in connection with the description of the nuclei tuberis.

If we now observe in the illustrations the location and extent of the different cell groups previously described and note also the character of their cells in the different mammals, we shall be prepared to understand the following description of the basal optic ganglion and the nuclei tuberis and the consideration of the relations of the latter two nuclei to the former.

GANGLION OPTICUM BASALE.

The name ganglion opticum basale was given with the intention of implying a function which this cell group almost certainly does not possess; on the other hand this name effectively distinguishes this cell group from the nuclei tuberis with which it has been confused. Since the so-called basal optic ganglion is such a characteristic cell group, and since the homologous groups in various mammals are so constant both as to location, extent and cell character, it appears highly probable that we shall not have to wait long before this name may be abandoned for one which will indicate its true function, and until then it seems better not to introduce a temporary name implying merely some morphological character. In arriving at the function of a cell group the first essential (and probably the most important of all) is to clearly distinguish it from the surrounding cell groups and to study carefully its relations to such cell groups; in this article I shall endeavor by means of illustrations and description to make the resulting picture of the so-called basal optic ganglion so definite that its confusion with all other cell groups will be impossible, and if this result be obtained there need be little concern as to the fitness of the name employed.

Location and extent of the ganglion opticum basale.

MAN.

The basal optic ganglion in man is a mass of gray matter, superficially situated partly in the tuber cinereum and partly in the anterior perforated substance, which extends along both borders of the optic tract. The main mass of cells forms in the anterior perforated substance a column which is closely applied to the dorsal portion of the oro-lateral surface of the optic tract. This mass is connected by a comparatively small number of scattered cells situated directly dorsal to the tract with another cell mass which follows in the tuber cinereum the caudo-medial border of the optic tract; in other words the basal optic ganglion consists, generally speaking, of two parallel columns of cells lying along either side of the optic tract, which are connected by scattered cells of the same type lying dorsal to the optic tract. For the second time I strongly recommend a consideration of pp. 39-40, where it is pointed out just what each type of illustration is intended to show.

Taking up the first series of man (Series AC) the basal optic ganglion appears caudally in Fig. 4 as a few scattered cells situated on the periphery of the tuber cinereum; Figs. 5 and 6 show the development of the cell mass as we pass orally. The cell masses shown in Figs. 4 and 5 are to be regarded as a caudal projection of the cell column lying along the caudo-medial border of the optic tract, and are continuous with the caudal portion of this cell column which appears first in Fig. 6. Between Figs. 6 and 7 is a considerable gap, in which the following changes have occurred: as the optic tract approaches the median plane and applies itself to the base of the brain the cell mass continues to increase in size, extending further laterally and also to a less extent further medially, and assumes a position as a column on the dorsal surface of the caudo-medial aspect of the optic tract, or in other words it extends in the tuber cinereum along the line where the tuber joins the optic tract. Midway between Figs. 6 and 7 the medial pole of the column crosses the median line and caudal to the optic chiasm unites with the corresponding column of the other side by means, however, of only a few scattered cells situated in the infundibulum. The next series (D) shows this fact. But still another change has occurred between Figs. 6 and 7, namely, after reaching its greatest development, which, as previously described, occurs at the juncture of the tuber cinereum with the caudo-medial border of the optic tract, the cell mass becomes rapidly diminished to only a few scattered cells which are situated on the dorsal (or deep) surface of the optic tract. Fig. 7 shows the extent of the basal optic ganglion slightly oral to this region of its poorest development; the section passes through the optic tract near its oro-lateral border and since the section is near this border the cell mass has increased in extent. Between Figs. 7 and 8 it increases steadily in size to reach its maximum in Fig. 8; this figure represents a section through the cell column which extends in the anterior perforated substance along the oro-lateral border of the optic tract. In Fig. 9 the basal optic ganglion has diminished in size, and this is due to a shortening of the lateral portion of the column; that the lateral portion of the column should be shortened is evident when we recall that the cell column lies parallel to the optic tract, and that the course of the optic tract is such that in the present plane of section as one proceeds orally the lateral portion of the tract appears and disappears first (see Figs. 1 to 10). Fig. 10 shows the most oral portion of the basal optic ganglion. The fact that the portion of the ganglion situated caudal (medial) to the optic tract does not extend as far laterally as that portion situated oral (lateral) to the tract should be correlated with the difference of the relation of the two borders of the tract to the base of the brain; for while the oral (lateral) border of the tract is in intimate relation to the anterior perforated substance from the chiasm to a point far lateral from the median plane, the caudal (medial) border of the tract is in intimate relation to the tuber cinereum, which extends for a shorter distance laterally, and then the tract passes over the crus cerebri, where of course it is no longer in relation to gray matter.

To sum up, Series AC of man (Figs. 4 to 10) shows, in sections almost parallel to the course of the optic tract, the appearance of the three parallel columns of cells which constitute the basal optic ganglion; one column lies in the tuber cinereum along the medio-caudal border of the optic tract, the second extends along the dorsal (deep) surface of the tract and consists of only a few cells, while the third and largest column extends in the anterior perforated substance along the latero-oral border of the tract. The caudal column is continuous in the infundibulum with the corresponding column of the opposite side. The figures show the inevitable relation of three parallel columns in slightly oblique section.

Series D of man (Figs. 11 to 18) shows essentially the same relations, but the plane of section is different. In the previous series the plane was almost parallel to the course of the optic tract, although slightly approaching the plane of a cross section; in Series D the plane of section is almost at right angles to the course of the optic tract, and both the caudo-medial and the oro-lateral borders are shown in all sections. It is evident that a plane of section at right angles to the median plane (which would cut both halves of the brain symmetrically) could not pass through the optic tract at right angles to its course, since the two tracts converge towards the median plane as they pass orally; therefore to obtain a cross section of the right tract the plane of section must lie more oral on this side than on the left. The asymmetry of the plane of section of Series D is not quite great enough to produce a cross section of the right optic tract, although this condition is very nearly attained.

When Fig. 11 of Series D is compared with Fig. 4 of Series AC the location of the basal optic ganglion is rather confusing, for in the latter series it appeared caudally in the tuber cinereum near the medio-caudal border of the optic tract, while in Fig. 11 it appears first in the anterior perforated substance along the oro-lateral border; if we keep in mind the asymmetry of the section, and the fact that the cell column here shown extends further laterally than the other two columns of the cell group and that in such asymmetrical sections the lateral portion is the most oral, little difficulty should exist in realizing just why this one of the three cell columns should appear first. Fig. 12 shows practically the same relations, except that the optic tract is nearer the median line. In Fig. 13 the cell column along the medio-caudal border of the tract, as well as the scattered cells dorsal to the tract, appears, and from here throughout the entire series these three columns are present. Of course all columns are in cross section. In Fig. 18 the cell mass is seen to extend across the median line, a condition which occurs also in the three other series of man. Series D (Figs. 11 to 18) shows clearly that the basal optic ganglion consists of two well developed parallel columns of cells connected by an intermediate parallel column consisting of only a few cells. As will be shown later the exact extent of the basal optic ganglion in all the mammals studied is readily determined by the distinctive histological character of its cells, and accordingly the three parallel cell columns have been considered as merely subdivisions of one nucleus, not because this seems convenient, but because the identical character of their cells makes such a conclusion unavoidable.

MACACUS RHESUS.

In macacus rhesus the basal optic ganglion is shown first in Fig. 22, although it extends slightly further caudally. In this figure the ganglion is situated just oral to the line of apposition between the tuber cinereum and the optic tract. In the sections between Figs. 22 and 23, as we pass orally, the cells become reduced in number and lie dorsal to the tract, and as the oro-lateral border of the tract is reached increase in number. In Fig. 23 appears the cell column which lies in the anterior perforated substance along the oro-lateral border of the tract. The further development of the ganglion (Figs. 24 and 25) needs no description. In Fig. 22 the medial pole of the ganglion is seen to approach the median line, and between Figs. 22 and 23, just caudal to the optic chiasm, a very few widely scattered cells unite the ganglia of opposite sides. As in man the basal optic ganglion in macacus is seen to consist of the same three parallel columns of cells, of which the oro-lateral column (situated in the anterior perforated substance) constitutes the greater part of the ganglion.

LEMUR RUFUS.

The basal optic ganglion of the lemur does not differ essentially from that of man and macacus, except that whereas in the two latter animals it consisted of two parallel cell columns loosely connected by a third, in the lemur this connecting mass of scattered cells (dorsal to the optic tract) is missing; consequently the ganglion consists of two entirely separate parallel columns of cells. Fig. 27 represents a section between the two cell columns. As in man and macacus the ganglia of opposite sides are united by a very few cells; this union occurs just caudal to the optic chiasm (slightly caudal to the level represented in Fig. 27).

CAT.

The basal optic ganglion in the cat (Figs. 31 to 35) has practically the same location and extent as in the lemur. As in the lemur the ganglion consists of the same two parallel cell columns, which are completely separate. Between Figs. 32 and 33 lies the region in which the ganglion is absent. Just caudal to the optic chiasm (caudal to level of Fig. 33) the ganglia of opposite sides are united in this series by a few cells; in the other two series of the cat no union was present.

Comparing the location and extent of the basal optic ganglion in all four animals the following facts should be noted:

1. The basal optic ganglion in all four animals consists almost exclusively (in some cases exclusively) of two compact, parallel cell columns. The larger of these two columns lies superficially in the anterior perforated substance along the line where this region becomes continuous with the oro-lateral border of the optic tract; the smaller column lies superficially in the tuber cinereum along the line where it joins the optic tract.

2. These two constant, parallel cell columns are united in man, and to a less extent also in macacus, by more or less diffusely scattered cells of the same type which lie dorsal to the optic tract.

3. In all four forms there occurs a union of the ganglia of opposite sides by means of diffusely scattered cells located just caudal to the optic chiasm. In man this union is very definite, in macacus less definite, while in the other two animals it is rudimentary and due to the presence of a very few widely scattered cells between the two ganglia. In the cat even this feebly developed fusion is not present in all individuals.

4. Although the phylogenetic series from man to the cat is too short to be of much service in revealing the phylogenetic development of so constant a cell group as the basal optic ganglion, it is apparent that as we descend the series the two parallel cell columns become separate (more closely united in man than in macacus, and separate in the lemur

and cat) ; the same is true as to the fusion of the ganglia of opposite sides (definite in man, less so in macacus, barely present in the lemur and not always present in the cat.)

Cell type of the basal optic ganglion.

It is not my intention to attempt to give in words the characteristics of the cells of the basal optic ganglion which have been already satisfactorily shown in the illustrations. I shall confine myself to pointing out the fundamental characters of these cells, and when we have thus become familiar with the main features of the cell picture we shall be in a position to discuss the relations of these cells to those of other groups. The water color reproductions of the cells of the basal optic ganglion, and of all other cells thus illustrated (Figs. 38 to 58), were all drawn from cross-sections of the brain. In Series D of man, in which the plane of section differs widely from that of a cross-section, I have been unable to observe any important difference in the appearance of the cells of the basal optic ganglion, and it is my opinion that the plane of section does not affect to any appreciable extent the appearance of the majority of these cells. The cells of the basal optic ganglion and of all other groups illustrated are as characteristic in Series D as in Series AC. However, I have not made a careful enough study of this point to state definitely that the cell character is absolutely unaffected by differences in the plane of section. The cells of the basal optic ganglion in all four animal forms (Figs. 38, 44, 50 and 55) are large polygonal cells which possess very coarse processes. These processes, as is shown in Fig. 37, form an intercellular feltwork; under low power one would hardly suppose that this feltwork was composed of cell processes, and the ganglion appears to be characterized not only by its typical cells but also by the presence of a distinctive intercellular substance. These processes are practically colorless, and are in Fig. 37 represented as blue because at this magnification they could not be shown in any other manner. The cell processes in Figs. 38, 44, 50 and 55 are not as long as they appear in the actual preparations. Another fundamental character of these cells is the distribution of the Nissl substance, nearly all of which is massed on the periphery of the cell; this peripheral distribution is not equal in all portions of the periphery, since the depth is much greater at certain points, and at other points of the periphery the Nissl substance may be almost entirely absent.

Of course the distribution of the Nissl substance will appear different according to the location of the optical section, and the figures show this to some extent, although they represent to a certain extent a combination of different optical sections. Although minor differences in cell character exist in different animals, the cell group is phylogenetically so old that in the relatively brief interval between man and the cat no changes in cell character have occurred which are sufficiently fundamental to permit of correlation with the phylogenetic position of the corresponding animals; this point will be discussed later in connection with the nuclei tuberis, where such a relation between cell character and the phylogenetic position of the corresponding animal actually exists. The structure of the cells of the ganglion opticum basale is such as to exclude the possibility of these cells being motor, whereas the large size of the cells probably indicates (as Dr. Donaldson has suggested to me) that they either receive impulses converging from many sources or distribute impulses over an extensive region.

Separation of the basal optic ganglion from surrounding cell groups through differences in cell character.

A subdivision of any portion of the nervous system based merely upon the splitting up of gray matter through the mechanical agency of fiber masses is, except in certain cases, valuable merely with reference to orientation; such a subdivision should therefore be considered as a crude (although necessary) beginning to be followed by a more careful study of the region involved in which the cell character of the various groups receives careful attention. Moreover it is highly unsatisfactory for an author to state dogmatically that he recognizes the presence of certain cell groups upon the basis of certain differences of cell character, concerning which he is either silent or else treats in a superficial manner; for we are left in doubt as to whether these differences in cell character are really fundamental, and as to the degrees of relationship between the cell characters of various cell groups. When we have described the location and extent of various cell groups and have made it possible to recognize this by means of a definite cell type, and when we have clearly shown the differences and similarities in cell character of various cell groups, and have pointed out the phylogenetic development and relations of these groups, then and not until then will there be a basis for experimental work which will help solve many important questions as to the elementary mechanisms of the nervous system. In the case of the basal optic ganglion, therefore, I shall not be content with having pointed out its location and extent, but shall proceed to compare the character of its cells with that of the cells of surrounding groups; such a comparison serves not only to set aside this cell group as different from other cell groups by virtue of differences in cell character, but it enables us also to recognize certain similarities of cell character between the cells of the ganglion and the cells of other groups, so that different degrees of relationship between the different cell groups may be provisionally stated.

I shall first point out the differences in cell character between the cells of the basal optic ganglion and those of the surrounding groups so as to complete the picture of this cell group; afterwards the relations of various cell groups will be discussed (but not until the nuclei tuberis have been described). There is no difficulty in distinguishing the cells of the basal optic ganglion from those of the nuclei tuberis and of the substantia grisea ventriculi tertii. This is shown by a reference to the corresponding figures 38, 39 and 40; 44, 45 and 46; 50 and 51; 55 and 56; moreover the difference between the cells of the basal optic ganglion and those of the substantia grisea is well shown in Fig. 37.

The cells of the basal optic ganglion may be readily distinguished also from those of the nucleus tubero-mammillaris, although both types of cells have a certain similarity; the failure to recognize the unity of the cell complex known as the nucleus tubero-mammillaris (mammillo-infundibularis) and to clearly separate it from the basal optic ganglion is one of the most important causes for our meager knowledge of this region. Considering first the relations of these two cell groups as to location, it is evident from the illustrations that they are closely related only for a short distance. Moreover the cells of the nucleus tubero-mammillaris are for the most part rather diffusely scattered, while those of the basal optic ganglion are densely packed together and the cell group is further characterized by the intercellular feltwork formed by the coarse colorless cell processes; these two points may be observed by comparing Figs. 36 and 37. Comparing the cell type of the two cell groups the fundamental difference found in all four animals involves the appearance of the Nissl substance; in both forms the Nissl substance is located principally on the periphery of the cell, but in the cells of the basal optic ganglion the massing of the Nissl substance on the periphery is extreme, whereas in the cells of the nucleus tubero-mammillaris the Nissl substance is not so densely packed together on the periphery and more of it is present in the central portion of the cell. In other words the Nissl substance in the cells of the nucleus tubero-mammillaris is more diffusely distributed throughout the entire cell. The difference in cell type obtains throughout the entire extent of both nuclei. A study of the illustrations shows that while other differences in cell type occur in certain animals the fundamental difference consists in the mode of distribution of the Nissl substance (Figs. 38 and 41; 44 and 47; 50 and 52; 55 and 57).

The separation of the basal optic ganglion from the nucleus paraventricularis hypothalami on the basis of cell type is difficult. Fortunately both are in all four animals sharply circumscribed, and although the extremities of these two cell columns approach one another (Fig. 10), they never actually fuse. A study of the location of these two cell groups will show their axes are almost at right angles to each other. In a former article I made the statement that the cells of the basal optic ganglion in man could not be distinguished from those of the nucleus paraventricularis, but a more careful study of the cell groups in man together with their study in other animals proves that this statement is not correct, although not far from the truth. As a matter of fact I have been unable to observe any one fundamental difference between these two types of cells which is clearly shown in all four animal forms, although in each animal some differences are present which always make a distinction possible. There is one difference which holds fairly well for all forms, and this is the same difference that was so evident between the cells of the basal optic ganglion and those of the nucleus tubero-mammillaris, namely, the Nissl substance is more densely massed on the periphery of the cell in the case of the basal optic ganglion, while in the cells of the nucleus paraventricularis the Nissl substance is more uniformly distributed throughout the cell. In man (Figs. 38 and 43) this difference is not marked, but in the basal optic ganglion (Fig. 38) the Nissl substance on the periphery forms in part large, irregularly placed masses of granules, while in the cells of the nucleus paraventricularis (Fig. 43) the granules are smaller, more uniform in size and do not stain so intensely; at the same time the central portion of the cell is somewhat more deeply stained (due to more Nissl substance) than in the case of the cells of the basal optic ganglion. Other differences in man are as follows: the cells of the basal optic ganglion are somewhat larger (the smallest cell illustrated in Fig. 38 shows only a small portion of a cell in optical section), the nuclear membrane is not so definite, and the nucleus is larger. In macacus (Figs. 44 and 49) the difference in distribution of the Nissl substance is less than in any of the other animals, but even here the Nissl substance in the cells of the basal optic ganglion is more nearly confined to the periphery, is denser here and not so dense in the interior portion of the cell as in the case of the other cell group; this results in a sharper differentiation between peripheral and central portions of the cell in the case of the basal optic ganglion. Other differences in macacus are: the cells and cell nuclei of the basal optic ganglion are smaller than those of the nucleus paraventricularis (the opposite is true in man), and the cells of this latter nucleus are rather piriform. In the lemur (Figs. 50 and 54) the difference in distribution of the Nissl substance is marked, the differentiation of the cell into peripheral and central portions being much sharper in the cells of the basal optic ganglion. In the cat (Figs. 55 and 58) the difference between periphery and center of the cell is again more marked in the cells of the basal optic ganglion, since in the cells of the other group the central portion of the cell (including the cell nucleus) stains deeply (Fig. 58). Note also in the cat that, just as in man, the cells of the basal optic ganglion are larger, but unlike those of man have smaller cell nuclei than the cells of the nucleus paraventricularis.

The resemblance of the cell type in the case of the basal optic ganglion and the nucleus paraventricularis hypothalami is therefore very close, but in all four animals studied the cells of the basal optic ganglion were found to be more sharply differentiated into a peripheral zone containing dense masses of Nissl substance and an inner portion relatively free from this substance, whereas in the cells of the nucleus paraventricularis hypothalami the Nissl substance was not so sharply differentiated as to its distribution. It will be recalled that within the cells of the nucleus tubero-mammillaris this differentiation was even less marked than within those of the nucleus paraventricularis.

Another cell group must be distinguished from the basal optic ganglion. This is the nucleus ansae peduncularis of Meynert (ganglion basale of Kölliker). It occurs in man, macacus and the lemur, but I was unable to find it in any of my three series of the cat. Its location and extent may be seen in the different illustrations. In all three animals in which it occurs it is readily distinguished from the basal optic ganglion by the large size of its cells. In man, as was pointed out by Kölliker, the cells of the ganglion basale may be readily separated from those of the basal optic ganglion by the fact that they are heavily pigmented (Fig. 42). In a previous article I have discussed the value of pigmentation as a basis of distinguishing different cell types. Yellow pigment occurs in certain nerve cells of the adult human and increases with age, but this occurrence and increase in amount is not erratic, but behaves differently with respect to different types of cells. Some types of cells never contain pigment, others always contain it, while still other types may contain none or under other conditions may contain a small or even a moderate amount. But however the total amount of yellow pigment in the brain of different adults may vary, the amount in each specific type of cell retains the same relation to that of every other type of cell; in other words, the relative amount of pigment in the different types of cells is constant in all individuals. Note that this pigmentation of the cells of the ganglion basale in man is accompanied by an additional characteristic (large size) and that the homologous cells of macacus and the lemur are entirely different from those of other cell groups, although pigmentation is of course lacking. This question of the relative amount of yellow pigment as a characteristic of certain types of cells which differ also in other respects will be noted again in connection with the nuclei tuberis. This yellow pigment should not be confounded with the brown pigment which occurs in the cells of the substantia nigra and elsewhere.

Now that the differences in cell type between the cells of the basal optic ganglion and those of surrounding groups have been studied it would be desirable to consider the relationship of these various cell groups from the standpoint of similarities in cell character. This consideration, as well as that of the literature, must however be postponed until the nuclei tuberis have been described, since such a comparison of the various cell groups demands a familiarity with the nuclei tuberis and the substantia grisea of the third ventricle.

NUCLEI TUBERIS LATERALES.

Under the name of nuclei tuberis laterales I shall describe certain cell groups of the pars optica hypothalami (telencephalon) which I have formerly considered very briefly in my monograph on the human diencephalon. Although a number of authors have written of nuclei tuberis, except in one case, there is absolutely no reason to believe that any of them have had in mind the characteristic nests of cells which will now be described. Kölliker undoubtedly saw these nuclei, although, as will appear later, his description is faulty and his figures incorrectly labeled; the result is so confusing that a careful study of this region is necessary to appreciate the value of Kölliker's observations. In the previous brief description I employed the name nuclei tuberis, but in the present article adopt the name nuclei tuberis laterales. The name nuclei tuberis is not distinctive and might be used to indicate any cell group whatsoever located in the tuber cinereum; as a matter of fact it has been so used, and the resulting confusion may be imagined when one considers how many different cell groups lie in the tuber cinereum. This confusion is not one merely of names, but involves the failure to distinguish (regardless of names) various cell groups of the tuber cinereum which in properly prepared material may be readily distinguished not only through differences in location but also through striking differences in cell type.

Location and extent of the nuclei tuberis laterales.

The nuclei tuberis laterales consist in man and macacus of several nests of cells located on the periphery of the tuber cinereum. In the lemur in this location one sees the beginning differentiation of these cell groups from the cells which surround them, although these differences are so slight that I have not attempted to show them in the illustrations. In the cat these cell groups are absent.

MAN.

In Series AC of man the nuclei tuberis laterales are shown in Figs. 1 to 8; the size of the cells, however, has been so much reduced that they should be examined with the aid of a hand lens. In Fig. 1 two indentations are shown on the base of the brain which should be noted. One indentation marks off on the base of the brain the medial boundary of the pes pedunculi, while the more medial indentation forms the superficial boundary between the tuber cinereum and the nucleus tubero-mammillaris (nucleus mammillo-infundibularis), this nucleus lying between these two fissures. The area bounded by these two fissures ventrally, and by the columna fornicis dorsally, is of especial importance in describing the location of the nuclei tuberis.

On examining Figs. 1 to 6 these two fissures are seen to be practically parallel, and the area bounded by them and by the fornix column undergoes as we pass orally the following change: in the caudal portion (Fig. 1) this area is occupied by the cells of the nucleus tubero-mammillaris, whose caudal pole constitutes the lateral ganglion of the mammillary body; passing further orally these large cells are replaced (especially those situated ventrally and medially) by the small cells of the nuclei tuberis laterales and of the substantia grisea. Accordingly the caudal portion of this region is continuous with the lateral ganglion of the mammillary body, whereas orally it gradually becomes the lateral portion of the tuber cinereum. In this region included between these two fissures ventrally, the pes pedunculi laterally, and the fornix column dorsally, lies by far the greater portion of the cells of the nuclei tuberis laterales. Referring to Figs. 1 to 8 the location and extent of these cell groups are evident, and only a few comments will be necessary. The nuclei tuberis laterales consist of a variable number of well circumscribed nests of small cells, and can be distinguished even without the aid of their characteristic cell type. These different cell nests are more or less connected with one another, and their separation is to be regarded probably as dependent upon the mechanical influence of fiber masses, since their partial fusion, identical cell type, and variable number would seem to exclude the possibility of these separate groups having different functions. The cell nests of the nuclei tuberis laterales are practically free from cells of surrounding groups.

In considering the second series of man (Series D, Figs. 11 to 15) it is absolutely essential to understand the plane of section; this has already been described in considering the basal optic ganglion. It will suffice to point out that Series D differs from Series AC in that the plane of section of the former passes more caudally as it passes from dorsal to ventral; and that in it the opposite sides of the brain are cut asymmetrically, in that the lateral portion of each section of Series D is situated further oral than the medial portion of the corresponding section. As was previously noted the plane of section of Series D is the only one which can pass through the right optic tract at right angles to its long axis; this relation to the optic tract will render a clear picture of the plane of section relatively easy. Bearing this plane of section in mind a study (with the aid of a hand lens) of Figs. 11 to 15 will show that the location of the nuclei tuberis laterales in Series D is practically the same as in the preceding Series AC, Figs. 1 to 8. Of the two fissures referred to previously, the lateral (just medial to the pes pedunculi) does not occur, since the obliquity of the plane of section is such that it appears only in sections situated further caudally. The medial one of these two fissures, however, appears in every section from Figs. 11 to 15, and as in the other series, forms superficially the medial boundary of by far the greater portion of the nuclei tuberis laterales.

MACACUS RHESUS.

In macacus the location of the nuclei tuberis laterales is similar to that in man, except that in most sections only one cell group is shown, and the cell mass does not invade the medio-ventral portion of the tuber. A comparison of Figs. 19 to 22 (macacus) with Figs. 1 to 8 (man) will show that in both animals the nuclei differ but little as to location. The two parallel furrows on the base of the brain are shown in Figs. 19 and 20.

In both man and macacus the nuclei tuberis laterales have, accordingly, practically the same location, and by far the greater portion is situated in the previously described region; this region, bounded ventrally by the two parallel furrows, laterally by the pes pedunculi, and dorsally by the fornix column, is occupied caudally by the nucleus tubero-mammillaris, and the nuclei tuberis laterales displace this nucleus as one passes orally, and after the optic tract has fused with the tuber, the nuclei tuberis are continued orally in the angle between the pes pedunculi and the optic tract. Since the purpose of this paper is in part to give a foundation for experimental study, it should be noted that *the main cell mass of the nuclei tuberis laterales may be accurately located in the intact brain just beneath the surface of the most lateral portion of the tuber cinereum, between the two parallel furrows and just caudal (medial) to the optic tract.* In toluidin blue sections the nuclei may be distinguished as circumscribed, lightly staining areas by means of the unaided eye. As previously stated no trace of the nuclei tuberis laterales is present in the cat, while in the lemur they are indicated so faintly that it seems best not to attempt to represent them in the illustrations.

Separation of the nuclei tuberis laterales from surrounding cell groups through differences in cell character.

The nuclei tuberis laterales are readily distinguished from the surrounding cell groups not only in that they are sharply circumscribed cell masses having a constant location, but also through their characteristic cell type. A reference to Fig. 36 will serve as an introduction to the further consideration of the differences in cell character. On comparing the cell character of the nuclei tuberis laterales of man and macacus (Figs. 39 and 45) with that of the other cell groups shown in the illustrations it will at once be evident that this cell type differs radically from all others except that of the substantia grisea of the third ventricle (Figs. 40 and 46); this similarity is of importance, and its significance will be considered when the relationship of the various cell types is discussed. Comparing the cell type of the nuclei tuberis laterales in man (Fig. 39) and in macacus (Fig. 45) it is evident that aside from the presence of pigmentation in man (of course not to be expected in macacus) there is no essential difference. The fundamental characteristic of this cell type in both forms lies in the appearance of the cytoplasm, which contains an extremely small amount of Nissl substance in the form of fine granules; the relation of cell nucleus to cytoplasm in respect to volume is also practically the same, although in macacus the cytoplasm is relatively less, a change that is to be expected, as will appear later. In describing the cells of the nucleus ansae peduncularis (p. 18) I pointed out the fact that if two cell groups differ as to the amount of yellow pigment in their cells they will also differ in other respects, and that homologous groups in lower animals (where all pigmentation is absent) will also appear different. Accordingly the presence of densely packed yellow granules in the cells of the nuclei tuberis laterales of man is not the only distinctive characteristic of these cells, but is connected with other characteristics, common also to the homologous cells of macacus; these characteristics involve the appearance of the cytoplasm and make it possible to separate these cells without difficulty from those of surrounding groups. If we study the cell type of the substantia grisea in all four forms (Figs. 40, 46, 51, and 56) we find the cell type practically unchanged, since in all forms the cells of this group are characterized by the extremely small amount of cytoplasm and relatively large nucleus; in many cells the cytoplasm is almost absent, and one sees only a large nucleus and perhaps one or more cell processes.

Accordingly the cells of the substantia grisea may be readily separated from those of all portions of the nuclei tuberis laterales not only through their smaller size, but also through the minute amount of cytoplasm in relation to the size of the cell nucleus; however, on the border line between these two types of cells occur occasionally transition types, whose significance will be discussed later. The nuclei tuberis laterales must be sharply distinguished from certain regions of the substantia grisea in which the cells are more densely packed together than in other portions of the substantia grisea. Differences in the density of different portions of the substantia grisea may be seen in many sections, and very definite areas of closely packed cells are shown in Figs. 17, 22 and 24. While in such dense masses the cells are possibly somewhat larger than the remaining cells of the substantia grisea, I do not consider the difference in cell type clear enough to justify one in setting aside such dense cell masses as distinct nuclei. Whatever the significance of these denser cell masses of the substantia grisea, one fact is certain: they differ both in location and in cell type from the nuclei tuberis laterales; the radical difference between these two kinds of cell groups should be clearly recognized. Of course the structure of the cells of the nuclei tuberis laterales as well as that of the cells of the substantia grisea is radically different from that of motor cells, while the small size of both types of cells would indicate that the connections of each cell were very limited; this correlation between cell size and the extent of the connections of each cell has already been referred to.

Relationship Of The Various Cell Groups To One Another.

From the previous description of the various cell groups together with a reference to the figures showing their cell types, it will be evident that the cell groups herein considered fall naturally into two classes:

1. Those composed of small cells, including the substantia grisea, and the nuclei tuberis laterales, and

2. Those composed of large cells, including the basal optic ganglion, the nucleus paraventricularis hypothalami, the nucleus tuberomammillaris, and perhaps also the nucleus ansae peduncularis (ganglion basale).

Taking up the first class of nuclei a most interesting relation will be found to exist between the substantia grisea and the nuclei tuberis laterales. The cells of the substantia grisea are the most primitive of the hypothalamus. The constancy of cell type in all four animal forms would suggest this, but the strongest evidence is derived from the nature of the cell type. The cell type of the substantia grisea, with its scanty cytoplasm, resembles that of embryonic cells; it occurs often in invertebrates; it is the only type in the hypothalamus which approaches that of the neuroglia cells, and transition forms occur concerning which one is in doubt as to whether they are neuroglia cells or cells of the substantia grisea; the cells are most abundant near the ventricle from whose border all cells of the hypothalamus have arisen, while laterally they are replaced by more highly differentiated types of cells. It is by no means certain that all or even any of the cells of the substantia grisea are functional. That the cells of the nuclei tuberis laterales have arisen from those of the substantia grisea is certain; if we look in the lemur at the regions where in higher forms the nuclei tuberis laterales occur, we see that the type of cell is somewhat different from the surrounding cells of the substantia grisea; this difference increases in macacus, and still more in man, while in the cat there is no indication of any new group. It is thus evident that the most recent cell groups of the hypothalamus (nuclei tuberis laterales) have arisen directly from the oldest cell group (substantia grisea), and that new cell groups are not necessarily formed by the further histological differentiation of portions of cell groups which are already highly developed, thus resulting in a very highly differentiated cell type, but that on the contrary new cell groups may arise from cell masses which have remained primitive. In other words the fact that a cell group is of recent origin does not give any information as to the extent of its histological differentiation, since this differentiation depends also upon the development of the cell group from which the new group arises.

In considering the second class of cell groups in the hypothalamus, all of which are composed of large cells, the nucleus ansae peduncularis requires only a brief consideration. The cell type of this cell group differs considerably from that of other groups, and the nucleus is probably of much more recent phylogenetic origin, since I have not as yet been able to find it in the cat; in order to consider the relations of this cell group a study of the neighboring regions of the telencephalon will be necessary, and I shall content myself with having shown that it is clearly distinguishable from the basal optic ganglion, and with having given the relative location of both groups of cells.

Concerning the other three cell groups in this class (basal optic ganglion, nucleus paraventricularis hypothalami, and nucleus tubero-mammillaris), the phylogenetic series from the cat to man is far too short to give such satisfactory results as in the case of the nuclei tuberis laterales, since the former three groups are of much older origin; certain relationships may, however, be established. Of these three cell groups the basal optic ganglion is composed of cells whose type is by far the most constant in the different animal forms, and the volume of this cell group is reduced in the lower forms to a less extent than is true of the two other nuclei; moreover, while the cell type of the basal optic ganglion approaches closely that of the nucleus paraventricularis, there are no transition forms between its cell type and that of the nucleus tubero-mammillaris or that of the substantia grisea; finally the basal optic ganglion is almost entirely free from the invasion of neighboring cells. All of these considerations make it seem probable that of the three nuclei the basal optic ganglion is the oldest and most highly developed. Closely related to the basal optic ganglion is the nucleus paraventricularis; it is more reduced in size in the lower forms than is the basal optic ganglion; between its cell type and that of the nucleus tubero-mammillaris transition forms occur, and between its cells lie many cells of the substantia grisea. While these facts make it probable that the nucleus paraventricularis is possibly not so old a cell group as the basal optic ganglion, they enable one to state positively that the nucleus paraventricularis is related on the one hand to the basal optic ganglion and on the other to the nucleus tubero-mammillaris. The third cell group, the nucleus tubero-mammillaris, is like the nucleus paraventricularis much reduced in size in the lower animals; it differs strikingly from both the other cell groups in being not sharply circumscribed, but on the contrary is very diffuse, extending through a large portion of the hypothalamus; it is invaded accordingly by the cells of the substantia grisea to a much greater extent than is the nucleus paraventricularis. Finally the cell type of the nucleus tubero-mammillaris shows a transition on the one hand to that of the nucleus paraventricularis and on the other to that of the substantia grisea. Therefore the nucleus tubero-mammillaris, while related to the nucleus paraventricularis, is related to the substantia grisea in three ways: transition forms of cells occur, the cells of both groups are intimately intermingled, and both cell groups are widely and diffusely distributed. The nucleus tubero-mammillaris is therefore the least highly developed of the three groups (owing to its relation to the substantia grisea), but whether it is also the most recent group cannot be decided here; it might just as well be an old and relatively stationary group, and to decide this point a longer phylogenetic series must be studied.

The relationship of these various cell groups of the hypothalamus may be summarized as follows:

1. The substantia grisea ventriculi tertii is the oldest, least highly developed, and the most diffusely distributed cell group of the hypothalamus. From it have been differentiated at least two (and probably all) of the four cell groups that lie more or less embedded in it. Certain portions of the substantia grisea appear slightly different from the rest, in that the cells are here crowded closely together. Whether any or all of the cells of the substantia grisea take part in conducting nervous impulses, or whether this group serves merely as material from which more highly differentiated cell groups are formed, is not known.

2. From the substantia grisea at least two different cell groups have arisen; these two groups of cells have developed along diverging lines. One of these two types constitutes the nuclei tuberis laterales; it is by far the youngest cell group in the hypothalamus, the first indication of its presence occurring in the lemur. The second cell group which has developed from the substantia grisea is the nucleus tubero-mammillaris; its cell type differs radically from that of the nuclei tuberis laterales, and it is a much older cell group.

3. Along the same line as the nucleus tubero-mammillaris, and to a higher degree of histological differentiation, have developed the nucleus paraventricularis and the basal optic ganglion; the nucleus paraventricularis is intermediate between the other two nuclei. From such a short phylogenetic series as that from man to the cat it is impossible to determine whether all three of these nuclei have developed independently from the substantia grisea or whether the other two nuclei have developed from the nucleus tubero-mammillaris and thus only indirectly from the substantia grisea.

4. A more extensive series of animal forms should enable us to understand such relations better; but a study of such material cannot be expected to yield satisfactory results unless the different cell groups be distinguished and unless the question of the relationship as expressed by the cell type be borne in mind.

5. Valuable results may be expected also from a study of the histogenesis of these various cell groups as revealed in the later stages of development of the human brain; little, however, is to be expected from such material unless it be fixed and stained with reference to the demonstration of cell structure in the nervous system, and the methods usually employed are not well adapted to this purpose.

CONCLUSION.

I have described with the aid of illustrations the location and extent of the basal optic ganglion and nuclei tuberis laterales in four forms of mammals, and have shown their relations to the surrounding cell groups of the hypothalamus; moreover the cell types of these two cell groups have been shown to differ radically, and the differences in cell character have been pointed out through which one can readily and accurately distinguish each of these two cell groups from those which surround it. Accordingly the principal purpose of this study has been accomplished, namely, to prepare a foundation of such a character as to make further study possible. It is now possible to study in the same manner neighboring portions of the telencephalon, or to extend with relative ease the present study of the hypothalamus through a much longer phylogenetic series than the critical nature of this study has permitted; the relations of the various cell groups of the hypothalamus can be studied also from the standpoint of histogenesis; or the nature of the cell processes and the character of the nerve endings around the cells of each group may be determined. But the greatest use of this study is that it makes possible intelligent experimental investigation of the hypothalamus. Experimental workers have been inclined to pass over differences in cell character and to make little or no attempt to correlate cell function with cell character, and fail to clearly recognize a fact to which I have, in a previous article, called attention in the following words: "The histological character of a nerve cell is an indication of its function. Differences in connections with portions of the organism which differ merely in spatial relations do not involve a difference in the character of the nerve cells, but are associated merely with the *location* of the nerve cell; for instance, arm and leg muscles, flexors and extensors are all innervated by the same type of cell, although such differences in peripheral connections correspond to the differences in the position of the corresponding nerve cells." It is therefore evident that experimental work which determines the connections of various portions of a given region with different portions of the organism, without taking into consideration differences of cell character, fails to distinguish between differences of connection dependent merely upon *spatial* differences and those differences of connection which involve differences in *cell activity,* such cell activity being indicated, not only in the nervous system but in all portions of the entire organism, by a definite type of cell character. That these two aspects of the function of the nervous system might be successfully studied in the hypothalamus by the use of experimental methods has been the controlling factor in determining the nature of this article.

But in addition to preparing a foundation for experimental work an attempt has been made to partially analyze the different elements involved in the histological complex of each cell type and to note in homologous cell groups of various animals what elements of cell character are constant; moreover in different cell groups of the same animal those elements of the entire complex of cell character which are common to the cells of two or more groups have been noted, and by this means an attempt has been made to form a provisional, although crude, idea of the degree of functional relationship among the different cell groups. At first sight such an attempt might appear premature, or it might even seem as though the task of the histologist were finished when he had pointed out the existence and location of the various cell groups, and that the determination of the functional relations of different cell groups might be safely left to the experimental worker. Such a conclusion, however, is not justified. Many regions of the brain are so complicated as to make the results of experimental investigation extremely vague, and in more suitable regions it is only under fortunate conditions that we are informed of the functional relations of a cell group except that it plays some unknown part in a complex mechanism underlying a complex function. In solving the relations of the different components of the various mechanisms of the nervous system histology must play an important and perhaps the principal part, since in the nervous system, as in the rest of the organism, it enables us to locate and to correctly state the function of every cell group of one definite cell type, if the function of this cell type has in other cell groups been previously clearly shown; that, however, it is not self-sufficient is evident.

But the neuro-histologist has a much more difficult task than that of interpreting in a general way the differences and similarities of cell character in different cell types. The cell types of certain cell groups resemble one another through possessing certain features of cell character common to all, and on the other hand differ in respect to other features of cell character; that such similarities and differences of cell type are an indication of corresponding similarities and differences of function I have already clearly shown in two cases. I have shown (Am. Jour. Anat., 1913) that although the three different types of muscle are supplied by three distinct types of nerve cells (p. 2), these three types of nerve cells possess a fundamental similarity of cell character; accordingly the cell type varies as the cell function. In the second place I have shown (Anat. Rec., 1913) that all cells supplying striated muscle, whether directly (anterior horn cells, etc.) or more or less indirectly (large pyramidal cells, cells of Deiters' nucleus, etc.) possess certain fundamental features of cell character in common. This fundamental character makes its appearance in the first cell of any efferent chain which is set aside for the innervation of striated muscle and is present in all cells of such a series, however many neurones may intervene between the cell in question and the striated muscle fiber; on the other hand the cells in such a voluntary motor chain differ in relation to their position in the chain. It is thus evident that the particular group of elements of cell type which corresponds to the motor function of the cell may be distinguished from other elements of cell type which must correspond to the other known or unknown influences. The feature of cell character which corresponds to motor function is the arrangement of Nissl substance in relatively coarse, discrete bodies; while the large size (which is usually supposed to be common to motor cells) is not directly related to the motor function, but is an element of cell character which is probably (as stated previously) an indication of the extensive connections of the cell, in that such a large cell receives impulses from (sphere of reception) or sends impulses to (sphere of influence) a large territory.

Accordingly each type of nerve cell should be regarded not as distinct from all other types, but as the result of different influences (due to the various relations of the nerve cell to other neurones and to the other portions of the organism); when so viewed the manifold variations of cell type, including cells of the most diverse types, as well as those of extremely similar types, do not appear to offer insuperable difficulties, but on the contrary these confusing relations of cell types will enable us eventually to work out the details of various nervous mechanisms. After the simultaneous analysis, by the aid of many methods, of the histological characteristics and the functional relations of different types of cells, and after the recognition of the result of any given functional relation upon the histological character of the cell, the neurohistologist will be able to take a further step. He will not only determine one portion of the functional relation through the presence of certain features of cell character (which is already possible in the case of various types of motor cells), *but he will actually reconstruct the greater portion of the entire complex of cell function upon the basis of the presence in the cell of certain groups of histological characters the meaning of each of which has been determined independently in different cells.* A beginning has already been made in that we are able to dissociate in motor cells the characteristic structure (corresponding to the motor activity) and the cell size (corresponding to the spheres of influence and reception of the cell); these two dissociated elements of cell character may be employed independently in examining any type of cell in the entire nervous system. Such results can be accomplished only through work which demands the exercise of the greatest critical ability, but that they will be attained I am firmly convinced.

It is evident that no such results are yet possible in the case of the hypothalamus, since no information is available concerning the functions of any of its cell groups; I have been compelled therefore to draw very general conclusions as to the nearness of functional relationship between different cell groups, since these conclusions could at present be based merely upon greater or lesser resemblance of cell type. One conclusion as to the function of these cell groups is, however, possible. The basal optic ganglion, the nuclei tuberis laterales, the nucleus paraventricularis hypothalami and the nucleus tubero-mammillaris are composed of cells whose histological character indicates that they are not efferent, but are concerned in receiving and correlating incoming impulses; these cells do not possess the relatively large, discrete Nissl bodies characteristic of efferent cells. Moreover (as suggested by Dr. Donaldson) the small size of such cells as those of the nuclei tuberis laterales would seem to indicate that the connections of these cells were less extensive than those of the cells of the other three nuclei. But now that these various cell groups have been described experimental workers will be in a position to attack the problems involving the connections and general functional significance of each of these cell groups, realizing that differences of cell type in different cell groups cannot be ignored, since such differences, as in every portion of the organism, correspond to differences in cell function; we may then expect results in this region upon which may be based in turn the constructive neuro-histology outlined above.

To those who prefer to employ several different histological methods I shall point out the fact that the Nissl method as employed by me brings out very clearly the differences and similarities of cell type, and accordingly should with the aid of experimental work and of other histological methods suffice to give much valuable knowledge as to the real relations involved in any nervous mechanism. Every method of studying the nervous system has its advantages, and I have employed the Nissl method merely because of all methods it is the most valuable in giving a complete picture of the cell groups of the entire nervous system. To this peculiar advantage of this method, through which we can compare the histological character of all cell groups of the nervous system, I should like to direct especial attention. Such a complete picture of the cell groups of the nervous system would seem to offer a most favorable ground-work for assimilating to itself isolated facts observed by means of all other methods of studying the nervous system; without other methods (histological, experimental, etc.) it is of course of little value. (See last paragraph of introduction, p. 3.)

In my opinion the demands of such work are so exacting that each investigator who attempts to gain a picture of the cell groups of a large portion of the nervous system should confine himself, at least for the most part, to one method, and of all methods that of Nissl shows the cell structure in the clearest manner. It is not isolated cytological details obtained by many methods, nor is it the proof or disproof of the actual existence in the living cell of certain features of cell structure that will be of most importance in the above outlined constructive neuro-histology, but a thorough familiarity with the location, extent and cell type of the different cell groups of practically the entire nervous system, together with a most critical appreciation of the differences, similarities and transitions of cell type of all these cell groups; without such broad knowledge of the various cell groups, which must of course assimilate to itself isolated facts regarding the function and the connections of various cell groups directly and indirectly with one another, and facts regarding the number, character, and mode of termination of the cell processes of various cell types, without such a comprehensive knowledge upon which to build we could not hope to penetrate far into the exact relations of the individual neurones of the nervous system.

LITERATURE.

The literature on the cell groups of the hypothalamus has been of practically no assistance to me. In the first place I did not read it until I had worked out these groups in the human brain, and upon reading it found no reason for modifying my conception of this region. In the second place some of the articles are concerned with animal forms so far removed from those upon which I have worked that the recognition of homologous groups is by no means certain. Finally the descriptions of cell groups are often so inadequate and so little attention is given to the differences in cell type as to make the literature, except in rare cases, almost unintelligible; this is true especially in those articles which are concerned with the brain of man and the higher mammals. Accordingly the results of other workers on the cell groups of the hypothalamus have not been incorporated to any great extent into the body of this article, but are here appended for the sake of completeness; to treat the greater portion of the literature otherwise would render the subject of this article needlessly obscure. The following consideration of the literature is given for the benefit of those who wish to make a careful study of the region in question; accordingly it appears advisable not to give an abstract of the various articles, since the complete accounts must be read by those for whom the following consideration is intended. On the contrary I shall for the most part confine myself to a consideration of certain points, showing wherein certain accounts are correct and wherein erroneous, and wherein some descriptions are altogether unintelligible.

The description of the cell groups of the hypothalamus contained in my monograph on the human diencephalon has been referred to in numerous places in the text and a further reference is unnecessary.

In Stricker's Manual of Histology (American translation) Meynert gives a brief but fairly clear description of the basal optic ganglion; on p. 688 he says: "At the lateral border of the tuber cinereum lies the inferior optic ganglion, which is 1.5 mm. broad, and contains spindle-shaped cells 30 μ in length and 15 μ in breadth. It begins just above the optic commissure and stretches along immediately over the tractus opticus as far as the posterior border of the tuber cinereum, a distance of more than a centimeter. I regard, with Luys, this optic ganglion as a part of the tuber cinereum, because it projects downwards, in company with the latter, into the lamina cinerea, beyond the surface of the lamina perforata anterior, of which J. Wagner considers it to be a part, and because it extends farther backward than the latter. Like the tractus itself, however, it certainly follows the inner border of the anterior perf. space. On profile sections (Fig. 270, II′) this ganglion has a sickle-like shape, the concavity looking forward. According to Luys, the two ganglia touch at the median line, a fact which I have not been able to verify, etc." From this description and from a study of Fig. 268 it is clear that Meynert had in mind a cell group which has much in common with that described under the same name in the present article. The exact extent is, however, not clear, and we have no assurance that he distinguished between this cell group and the nucleus tubero-mammillaris, or that he included all portions of the basal optic ganglion. Moreover he was unable to observe the union of the ganglia of opposite sides, a fact which makes it almost certain that he failed to include the medial portion of each ganglion.

When we attempt to understand the article of von Lenhossék, in which he divides, in man, the basal optic ganglion of Meynert into a nucleus supraopticus and two nuclei tuberis, we are confronted with an impossible task. We are informed that all three nuclei are composed of small, spindle-shaped, multipolar nerve cells, as well as neuroglia; this is a most disturbing statement and renders it absolutely impossible to form any idea as to what cell groups the author had in mind. For by no means can the cells of the basal optic ganglion be termed small, since they measure up to 35 μ in diameter, and compared with the cells of the nuclei tuberis and the substantia grisea their large size is most evident (Fig. 37). Accordingly the word " small " would seem to make it certain that Lenhossék's nucleus supraopticus cannot be a portion of Meynert's basal optic ganglion; and yet after Meynert's description and illustrations it would seem remarkable for anyone to overlook such a prominent cell group as the oral portion of the basal optic ganglion. Again we are informed that the nucleus anterior of the tuber cinereum is the largest of all three nuclei (nucleus supraopticus and the anterior and postero-lateral nuclei of the tuber) " *und bildet eigentlich den Hauptbestandteil des Tuber*," and that apparently it reaches the median line. What can this mean? Can the " small " cells of this anterior nucleus be the large cells of the nucleus tubero-mammillaris, or is this nucleus a portion of the substantia grisea? One is almost tempted to infer from Lenhossék's description that his three portions of Meynert's basal optic ganglion are a complex of what I have described as the basal optic ganglion and portions of the nucleus tubero-mammillaris, all of which are composed of large cells, and that the cells of the substantia grisea he may possibly have considered neuroglia; since he employed the Weigert stain such a mistake is by no means improbable. But just what the three nuclei of Lenhossék represent is absolutely impossible to determine.

Kölliker's description of the nuclei tuberis and the basal optic ganglion I have in a previous article termed *vortrefflich;* this implies a uniform excellence which this description by no means possesses. It were more fitting to term Kölliker's account of these nuclei " remarkable," for it is remarkable as to insight into this complicated region, and at the same time remarkable for the contradictions, incorrectly labeled figures, and other faults which detract from its value. Only to one who has made a thorough study of this region is the difference apparent between the unintelligible description of von Lenhossék and the essential excellence of that of Kölliker, and from 1896 until 1910 no one has made himself sufficiently familiar with this region to realize the many excellent points in Kölliker's work. The real contributions of Kölliker are as follows:

Es müssen Nuclei tuberis von den Nuclei supraoptici unterschieden werden (p. 602)...*Die Nuclei tuberis kommen mehr in den medialen Gegenden vor, besitzen kleine Nervenzellen, etc.* (p. 603)...*Die Nuclei supraoptici haben grössere Zellen, etc.* (p. 603). Moreover Figs. 704 and 705 are correctly labeled and entirely intelligible. Fig. 702 shows the nuclei tuberis laterales excellently, but unfortunately they are termed "ganglia optica basalia"; on p. 599 these groups are correctly termed nuclei tuberis, while on p. 519 they are incorrectly termed (in text) "ganglia optica basalia." This uncorrected error in Fig. 702 is unfortunately characteristic of the inconsistent nature of Kölliker's description. But in Fig. 631 we meet a further difficulty, since the cell mass of the tuber which in Fig. 631 (rabbit) is termed "Ganglion opticum basale" is stated on p. 603 to represent the "Ganglia tuberis"; in reality this cell mass is simply a portion of the substantia grisea and is not the nuclei tuberis laterales (which are shown in Figs. 702, G. o. b., and 705, G. t.). On p. 599 he has incorrectly stated that the nuclei tuberis are continued more or less definitely into two of the groups of the corpus mammillare, nucleus intercalatus (or possibly a separated portion of the medial nucleus as discussed in my monograph on the diencephalon) and the nucleus tubero-mammillaris; this proves beyond doubt that Kölliker's nuclei tuberis are to be regarded as topographical groups rather than determined by a definite cell character. On the other hand he has confused a portion of the nucleus tubero-mammillaris with the basal optic ganglion; on p. 600 he says: *Dieser Kern ist schon in der Fig. 703 in der Grenzlage zwischen dem Tractus opticus, dem Reste des Pes pedunculi und dem Nucleus Tuberis lateralis in den ersten Anfängen vorhanden und zwar wie in der Linsenkernschlinge drin, wird aber nach vorn immer grösser, etc.* Accordingly Kölliker has included portions of the nucleus tubero-mammillaris with the nuclei tuberis on the one hand, and on the other with the basal optic ganglion. The vacant space surrounding the third ventricle in his figures raises the question as to how he regarded the substantia grisea of the third ventricle; its relations to the other nuclei he has failed to point out, and in how far he confused this cell mass with the nuclei tuberis we cannot determine, except in Fig. 631 in case of the rabbit, where this error is apparent; this cell group of the rabbit is the substantia grisea and does not correspond to the nuclei tuberis as shown in his figures of man. In conclusion, Kölliker's description and figures are often very faulty, but on the other hand in his figures may be recognized in many cases cell groups correctly represented.

Cajal (pp. 756-757) describes in rodents a cell group under the name *ganglio peri-kiasmático o tangencial* which without doubt is homologous with the basal optic ganglion of higher mammals. He is in doubt as to whether it corresponds to the supraoptic nucleus of Lenhossék and the supraoptic complex of Kölliker. As previously explained it is impossible to identify the supraoptic nucleus of Lenhossék, especially since he says that it is composed of "small" cells; the description of Cajal as well as his excellent illustration (Fig. 640) shows that the *ganglio peri-kiasmático* is composed of large cells. Cajal further states that there is a great difference in form, position and extent between this ganglion of rodents and the above human centers. While I have not yet studied the basal optic ganglion in rodents I am strongly of the opinion that this ganglion in rodents does not differ essentially either in form, position or extent from the basal optic ganglion in man; I base this conclusion on the constancy of this ganglion from man to the cat, and upon Cajal's description and illustration. There is no difficulty in recognizing that the centers, which Cajal describes in the tuber under the names of anterior, posterior and superior nuclei of the tuber, are portions of the substantia grisea and have nothing to do with the nuclei tuberis laterales of man and macacus; the difference in location of these three nuclei and the fact that there is every reason to believe that the nuclei laterales are not present in the rodents (appearing first in the lemur) renders confusion impossible. Under the name *núcleo subventricular* Cajal describes (p. 731) a cell column which is beyond doubt homologous with the nucleus paraventricularis hypothalami, which I have described in man and the higher mammals; Cajal's description and illustration (Fig. 604, T) place this fact beyond the possibility of a doubt. Accordingly Cajal's description of the hypothalamus enables us to recognize positively two characteristic cell groups in rodents one of which is homologous with the basal optic ganglion and the other with the nucleus paraventricularis hypothalami of higher animals. Concerning the complex of the nucleus tubero-mammillaris we are left in doubt.

The presence of the basal optic ganglion and the nucleus paraventricularis is certain not only in rodents but even in the marsupials, as is seen from Ziehen's description of the brain of Pseudochirus peregrinus. In describing Fig. 28 he says (p. 713): *Sehr schön ausgeprägt ist beiderseits das Ganglion opticum basale (nucleus supraopticus). Rechts sendet es einen langgestreckten Ausläufer in das Pedamentum laterale. Ingesammt erstreckt es sich über 1.3 mm. in sagittaler Richtung. Seine Zellen messen 21 μ. Frontalwärts reicht es noch ein wenig über den vorderen Chiasmarand hinaus. Einen Zerfall in mehrere Zellgruppen, wie ihn Lenhossék und Kölliker bei dem Menschen beschrieben haben, vermöchte ich nicht sicher nachzuweisen.* On p. 714 in describing this same section (Fig. 28) Ziehen says: *In der grauen Masse zu beiden Seiten des 3 Ventrikels kann man—in der Reihenfolge von unten nach oben—folgende Theile unterscheiden. Unmittelbar oberhalb des Chiasmas folgt der kleinzellige Nucleus tuberis* (evidently the substantia grisea), *auf diesen ein gross-zelliger lateraler Kern, in welchem der Fornixsäule eingebettet ist* (a portion of my nucleus tubero-mammillaris), *und ein eben so grosszelliger medialer Kern, welcher der Ventrikelwand unmittelbar anliegt.* This latter nucleus is evidently homologous with the nucleus paraventricularis hypothalami, and I thoroughly agree with Ziehen when he continues as follows: *Bei der sehr starken Ausprägung des letzeren war ich sehr erstaunt, eine ähnliche Bildung bei anderen Säugern nirgends beschrieben zu finden. Ich will den Kern einstweilen als Nucleus subcommissuralis bezeichnen.* Ziehen's illustrations unfortunately show almost nothing of the various cell groups, but his concise description is most valuable.

Worthy of special notice is the valuable contribution of Friedemann entitled *Die Cytoarchitektonik des Zwischenhirns der Cercopitheken mit besonderer Berücksichtigung des Thalamus opticus.* As the title indicates more attention is paid to the thalamus than to the hypothalamus, although both the pars mammillaris and the pars optica are by no means neglected. In this article Friedemann takes into consideration my monograph on the human diencephalon. To consider intelligently Friedemann's account of the cell groups of the hypothalamus it is necessary to realize that his chief purpose is to subdivide this region into topographical cell groups, which are not necessarily composed exclusively of one type of cell, but may represent complex centers formed by the overlapping of several primary nuclei; on the other hand he has occasionally divided a cell mass, composed of cells of the same type, into subgroups whenever factors other than cell character (such as number and grouping of cells) would permit. In this he has consistently endeavored to give us a topographical subdivision into as many areas as may possibly be distinguished in cell preparations. It is accordingly evident that my cell groups (primary nuclei) have been set aside in virtue of the possession of one type of cell which corresponds to some known or unknown cell function or functions and that the topographical value of my work is primarily concerned with the location and distribution of such a single cell type; and on the other hand it is evident that Friedemann's subdivision, not being confined to this one criterion of cell character, results in a much more minute subdivision which is of great value in exact orientation, and that his cell groups may represent primary nuclei, portions of such nuclei, or complex nuclei, according to the criteria employed in the establishment of each cell group. Apparently Friedemann has not grasped this fundamental difference in our aims, since (p. 312) he says: *So wichtig auch u. a. die von Malone festgestellte Tatsache ist, dass im Thalamus opticus keine Zellen vom motorischen Typus vorkommen, so sehr wir auch in vielen Einzelheiten mit diesem Autor übereinstimmen, als topographisches Einteilungsprinzip können wir seine Methode nicht anerkennen.* It is certainly my earnest desire that no one should consider the method I have employed as a *topographisches Einteilungsprinzip,* since I myself have never so considered it, and had supposed that I had made this fact evident. But Friedemann's work is something more than a pure topographical subdivision, since he has informed us as to whether a cell group has been recognized on account of its cell type, or whether it is differentiated from the surrounding cells on the basis of other criteria; in other words he has, in giving us this minute and most valuable topographical subdivision, not lost sight of the distribution of the various cell types. The fact that Friedemann and myself have subdivided the diencephalon from different points of view is a fortunate circumstance, and the difference in results is to be expected and welcomed. Other subdivisions from other standpoints are desirable, but it is essential that we be accurately informed just what criteria have been employed in setting aside each cell group; and moreover we should carefully distinguish between such cell groups of different authors as are identical and such as do not entirely correspond.

Taking up the various cell groups of the hypothalamus, Friedemann describes the nucleus intercalatus corporis mammillaris and the nucleus paraventricularis just as I had found them in man, and he adopts my names for them. He also adopts my name " nucleus mammillo-infundibularis "; I have previously in this article pointed out that this name must be changed, and have adopted instead that of nucleus " tubero-mammillaris." But it is not clear to me that Friedemann has included all the cells in this group which I have assigned to it; unfortunately the illustrations (photographs) are of little value in showing the distribution of each cell type. It is certain that his nucleus posterior pedamenti lateralis (Fig. 9, Plp) is a portion of my nucleus tubero-mammillaris; moreover Friedemann has called attention to the fact (p. 367) that his lamina grisea separans (Fig. 9, lgs) is a portion of this same nucleus. Such subdivisions are of course desirable for their topographical value, but the common cell character should be kept in mind. In considering the basal optic ganglion Friedemann has fallen into the same error that I did in my monograph on the diencephalon, and for the same reason, since both of us were not primarily interested in the telencephalon; this error consists in considering merely the cell mass which follows the oro-lateral border of the optic tract as constituting this ganglion. It is certain that to the basal optic ganglion of cercopithecus must be added Friedemann's " nucleus anterior pedamenti lateralis " (p. 370 and Fig. 11, Pla) as well as his " stratum supraopticum " (p. 369 and Fig. 9, Sso.). That these two cell groups belong to the basal optic ganglion is clear both from the descriptions and illustrations. It is unfortunate that neither the cross sections nor the horizontal sections illustrated give the region just caudal to the optic chiasm. Friedemann's cross sections may be best compared with my Series D of man (Figs. 11 to 18) since the plane of section is similar; in comparing these two series it is evident that the most oral section (Fig. 11) of Friedemann stops short of a most important region of the basal optic ganglion. Again his first horizontal section (Fig. 12) likewise fails to give this region near the optic chiasm. (The omission of this region is only natural, since Friedemann's article deals primarily with the diencephalon.) Accordingly I see no reason to believe that the basal optic ganglion in cercopithecus is essentially different from that in other animals from man to the marsupials.

In Friedemann's description of cercopithecus I am unable to find any cell groups which would correspond to the nuclei tuberis laterales, and unfortunately the illustrations are of such a nature (photographs) as not to reveal the presence of such groups. It is not probable that the nuclei tuberis laterales are wanting in cercopithecus, since they are present in macacus and are indicated even in the lemur; their presence, if indeed they occur in cercopithecus, might easily be overlooked unless one had seen them in man, where these nests of cells are very definite. The fact, which

Friedemann himself has pointed out (p. 367-8), should be most carefully noted: Friedemann's nuclei of the tuber cinereum are different portions of the substantia grisea; he calls attention moreover to the fact (p. 367) that the substantia grisea has been divided into these nuclei rather on account of topographical relations and differences in the crowding together of cells than on account of differences in cell form. Accordingly these topographical cell groups of the substantia grisea must not be confused with the nuclei tuberis laterales, since the latter are composed of cells of another type.

BIBLIOGRAPHY.

CAJAL, S. R. Y: Textura del sistema nervioso, etc., 1904, vol. 2.

FOREL, A.: Beiträge zur Kenntnis des Thalamus opticus, etc. Gesammelte hirnanatomische Abhandlungen, 1872, pp. 17-43. (Published originally in Bd. 66 der Sitzb. der k. Akad. d. Wissensch. in Wien, dritte Abteilung, Juni.)

FRIEDEMANN, M.: Die Cytoarchitektonik des Zwischenhirns der Cercopitheken, etc. Jl. f. Psychologie u. Neurol., 1911, XVIII, Ergänzungsheft 2.

GANSER, L.: Vergleichende anatomische Studien über das Gehirn des Maulwurfs; Morpholog. Jahrbuch, 1882, VII.

KÖLLIKER, A.: Handbuch der Gewebelehre, 1896, II.

VON LENHOSSÉK, M.: Beobachtungen am Gehirn des Menschen, Anat. Anz., 1887, II, Nr. 14.

MALONE, E.: Über die Kerne des menschlichen Diencephalon. Aus dem Anhang zu den Abhandlungen der königl. preuss. Akad. d. Wissensch., 1910.

Observations concerning the comparative anatomy of the diencephalon. Anat. Rec., 1912, VI, No. 7.

Recognition of members of the somatic motor chain of nerve cells, etc. Anat. Rec., 1913, VII, No. 3.

The nucleus cardiacus nervi vagi, etc. Am. Jour. Anat., 1913, XV, No. 1.

MEYNERT, TH.: The brain of mammals. Stricker's manual of histology (American translation), 1872.

ZIEHEN, TH.: Das Centralnervensystem der Monotremen und Marsupialier. Teil 2, erster Abschnitt. From Semon's Forschungsreisen, III.

EXPLANATION OF ILLUSTRATIONS.

Figs. 1 to 35 and 1A to 35A have been prepared in the following manner: The entire section was in each case projected at a magnification of ten diameters, and the outlines together with as many details as possible were drawn in pencil; even bloodvessels, tears in the section, particles of detritus, etc., were drawn in so as to serve the purpose of orientation. Under the microscope at the same magnification (ten diameters) the drawing was completed, with the occasional aid of higher magnification. (Of course the drawings were not begun until I had a clear idea of the location, extent, cell character, and relations of the various cell groups.) This completed drawing is not used for publication but serves as the basis for two others. In the first place an outline drawing is made (by tracing) and the various structures labeled (Figs. 1A to 35A); in these drawings a rectangular area is indicated which contains the region in which we are interested. A second series of drawings (Figs. 1 to 35) are traced from that portion of the original included within the rectangular area, and the details filled in, under control of the microscope. Finally these two series of drawings have been reproduced in parallel columns; in order to do this the outline drawings have been more greatly reduced in size than the detailed drawings, the resulting magnification being indicated in the explanation of each plate. Figs. 1 to 18 have been so much reduced that they should be examined with the aid of a hand lens; the cells of the nuclei tuberis laterales are especially difficult to recognize without such aid.

It is important to understand just what these drawings are intended to illustrate. The outline series (Figs. 1A to 35A) needs no explanation, except the statement that the size and relations of the structures shown have been accurately reproduced. In the other series (Figs. 1 to 35) the distribution of each cell group is accurately shown, each being indicated by one type of cell which may be distinguished in all drawings from the cells of all other cell groups; thus different cell groups may be distinguished when their cells are intermingled, and it is thereby possible to reproduce the actual extent of each cell type without resorting to an arbitrary boundary. On the other hand in order to indicate differences in cell type it has been necessary to make the cells much larger than they appear at such a low magnification, and this in turn involves a reduction in the number of cells. However, the relative density of each cell mass in its various portions is shown, and the relative size of different cell types has been maintained, although this difference in size has in some cases been somewhat exaggerated in order to make it more obvious. For a true picture of each cell type one must study Figs. 38 to 58, in which each cell type has been reproduced exactly as it appears.

The exact cell size and distance between the cells of the nuclei tuberis laterales and the basal optic ganglion, as well as that of the surrounding cell groups, has been reproduced exactly in Figs. 36 and 37, which also show the different cell types as they appear at a relatively low magnification. These two illustrations (Figs. 36 and 37) will be explained on the pages facing them.

Figures 38 to 58 were drawn as follows:

With the aid of the camera lucida the cell outlines and as many details as possible were drawn in pencil. Then under control of the microscope the exact appearance of the cells was reproduced in water color. Each cell is to be regarded as an individual and the spatial relations of the cells in each figure do not correspond to those between the cells of the corresponding cell group in the preparations. In these figures the cells have been reproduced by combining to a certain extent different optical sections of the same cell. All cells have been drawn at a magnification of 580 diameters, and have been reproduced without reduction. Figs. 38 to 58 were all drawn from cross-sections of the brains of the various animals. In Series D of man the plane of section differs widely from that of a cross-section, and yet (without making a careful study of this point) I was unable to observe that this difference in the plane of section was correlated with any difference in the appearance of the cell types here illustrated. On the contrary I can state positively that each of the above types of cells was as characteristic in Series D as in Series AC, and that differences in the plane of section could not possibly lead to a confusion of the different cell types.

PLATE IV.

HOMO. SERIES AC.

Magnification of Figs. 1 to 4 = 5 diameters.
Magnification of Figs. 1A to 4A = 2 diameters.

● = Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the corpus hypothalamicum (Luysii).

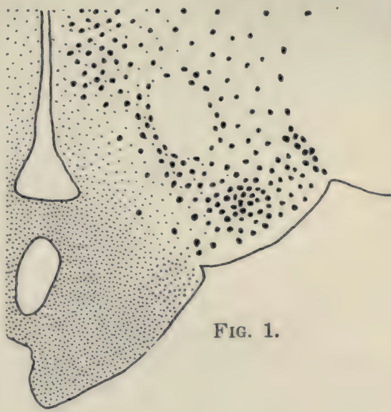


FIG. 1.

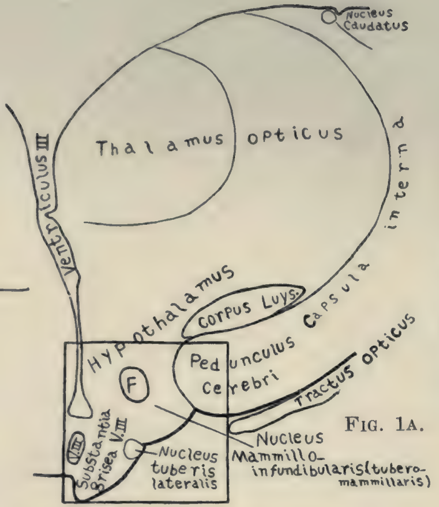


FIG. 1A.

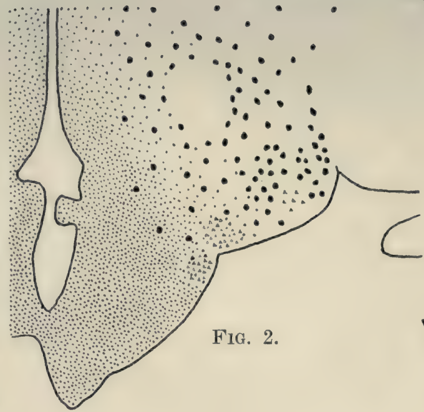


FIG. 2.

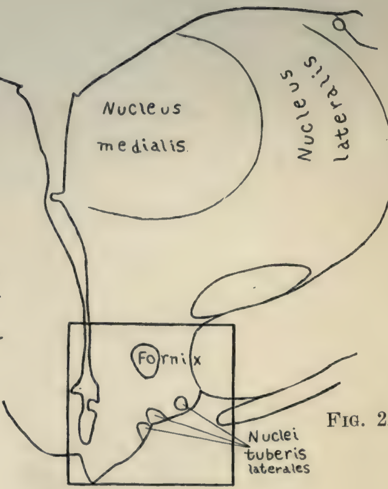


FIG. 2A.

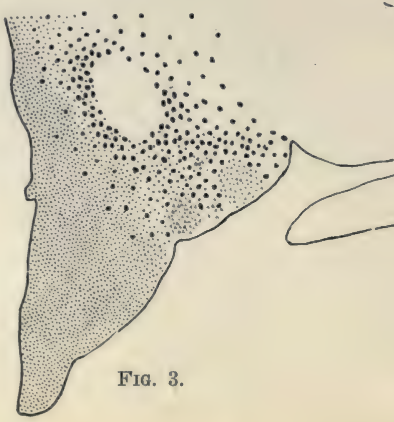


FIG. 3.

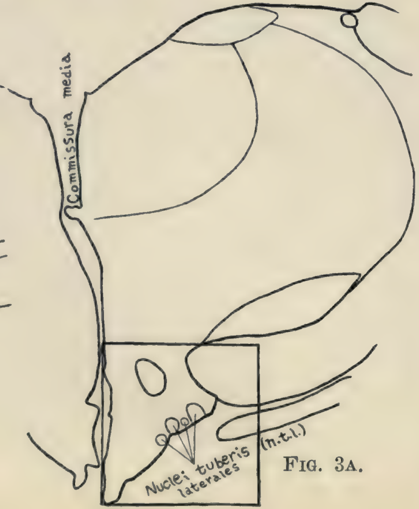


FIG. 3A.

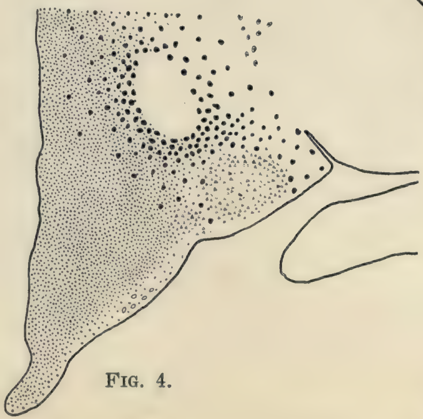


FIG. 4.

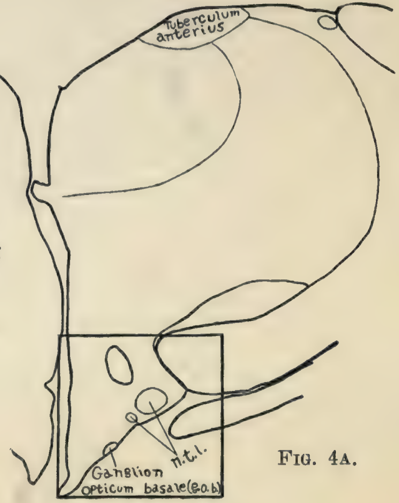


FIG. 4A.

PLATE V.

HOMO. SERIES AC (CONTINUED).

Magnification of Figs. 5 to 7 = 5 diameters.
Magnification of Figs. 5A to 7A = 2 diameters.
● = Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the corpus hypothalamicum (Luysii).

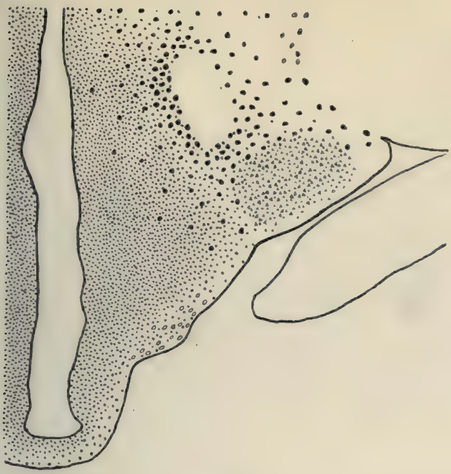


FIG. 5.

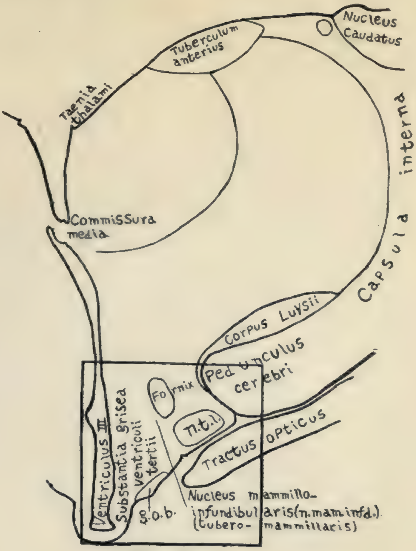


FIG. 5A.

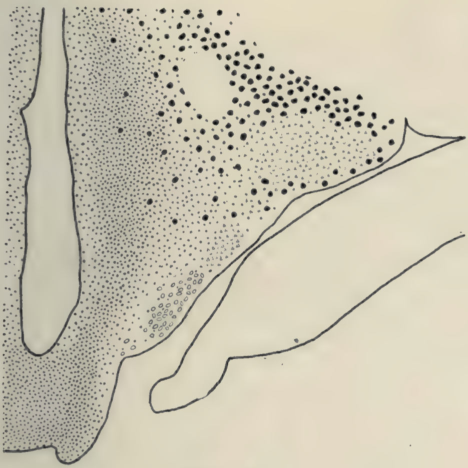


FIG. 6.

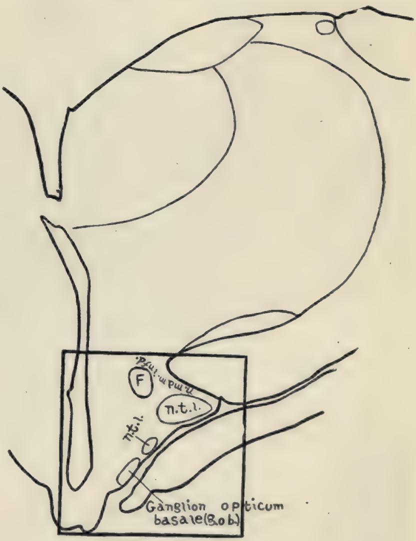


FIG. 6A.

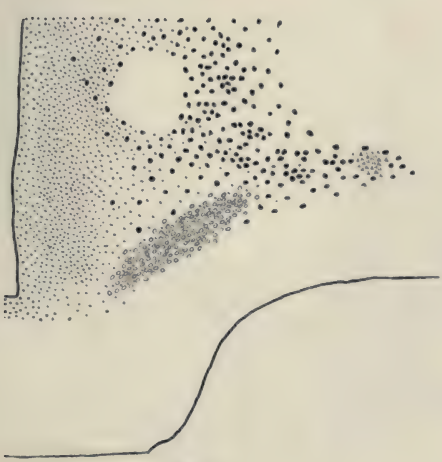


FIG. 7.

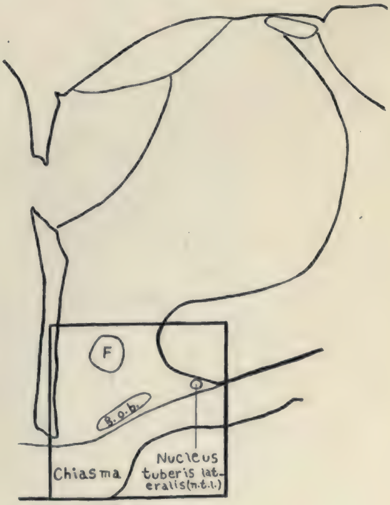


FIG. 7A.

PLATE VI.

Homo. Series AC (Concluded).

Magnification of Figs. 8 to 10 = 5 diameters.
Magnification of Figs. 8A to 10A = 2 diameters.

● = Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami.
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the nucleus ansae peduncularis (ganglion basale of Kölliker).

Note that the cells of the nucleus tubero-mammillaris and those of the nucleus paraventricularis are represented by the same type of cell; moreover the same type of cell has been employed to represent the cells of the corpus subthalamicum and those of the nucleus ansae peduncularis. It seems advisable to use one type of cell to represent the cells of two different groups, when these two groups are clearly distinguishable topographically, rather than to multiply the number of symbols used, and thus render it more difficult to distinguish between them. The outline drawings will make a confusion of such cell groups impossible.

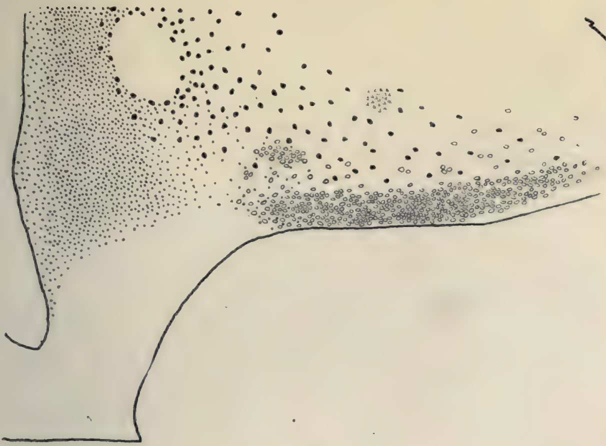


FIG. 8.

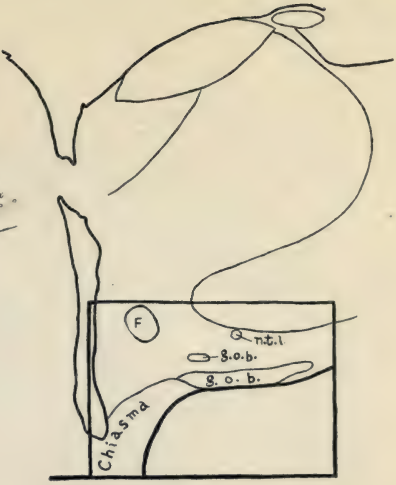


FIG. 8A.

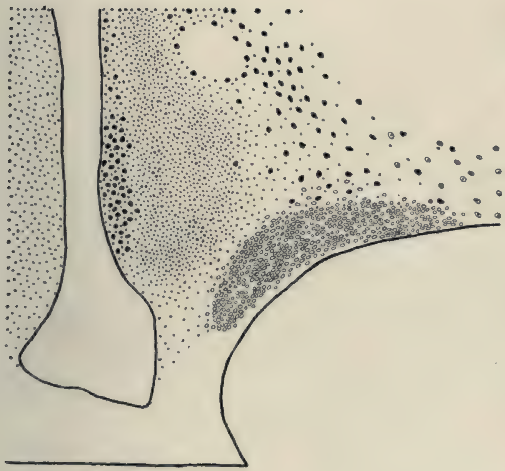


FIG. 9.

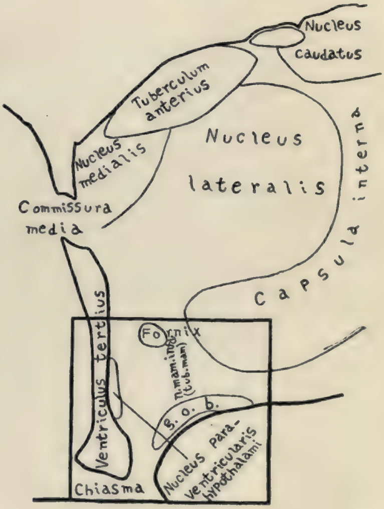


FIG. 9A.

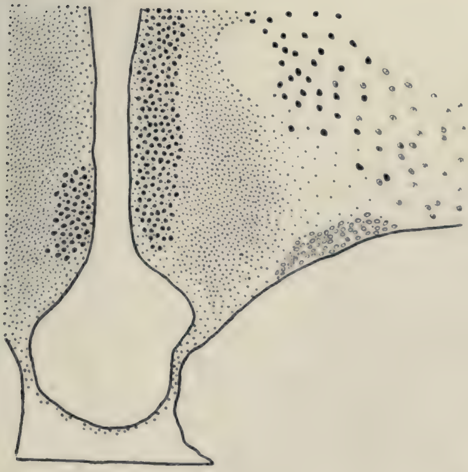


FIG. 10.

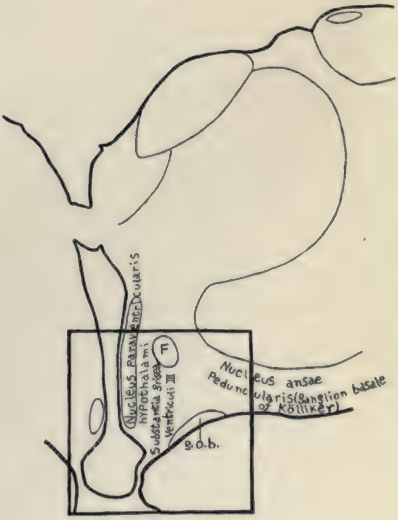


FIG. 10A.

PLATE VII.

Homo. Series D.

Magnification of Figs. 11 to 14 = 5 diameters.
Magnification of Figs. 11A to 14A = 2 diameters.
● = Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
• = Cells of the substantia grisea ventriculi tertii.
▷ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the nucleus ansae peduncularis.
° = Cells of the ganglion mediale corporis mammillaris.
▶ = Cells of the nucleus intercalatus corporis mammillaris.
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

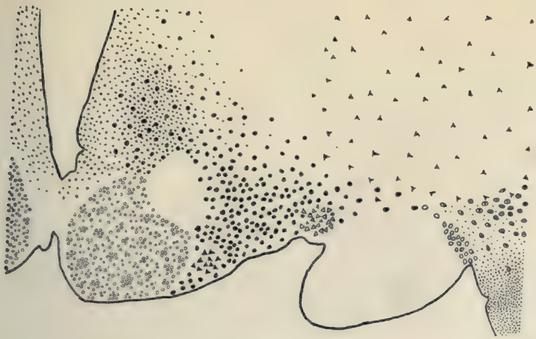


FIG. 11.

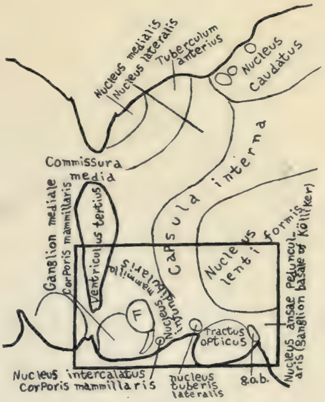

Nucleus medialis
Nucleus lateralis
Tuberculum anterius
Nucleus caudatus
Capsula interna
Commissura media
Ganglion mediale corporis mammillaris
Ventriculus tertius
Nucleus mammillo-infundibularis
Nucleus lentiformis
Nucleus ansae peduncularis (Ganglion basale of Kölliker)
F
Tractus opticus
Nucleus intercalatus corporis mammillaris
nucleus tuberis lateralis
g.o.b.

FIG. 11A.

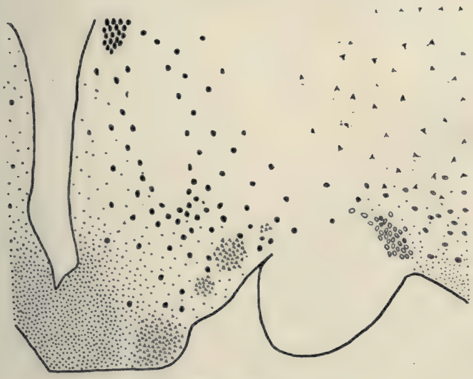


FIG. 12.

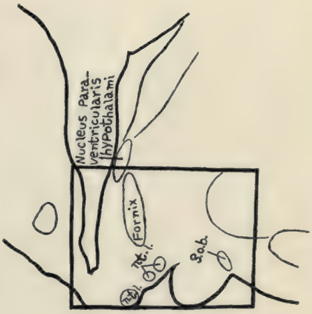


FIG. 12A.

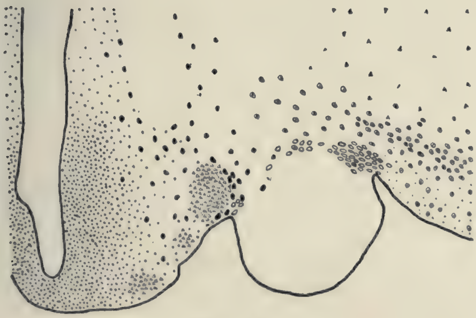


FIG. 13.

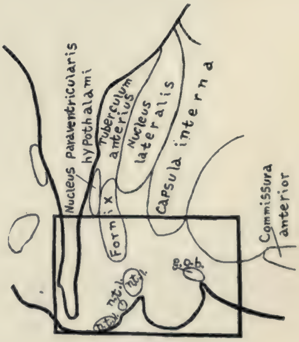


FIG. 13A.

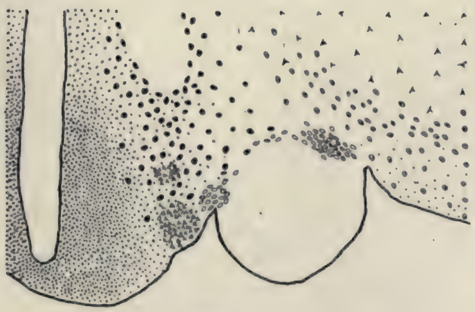


FIG. 14.

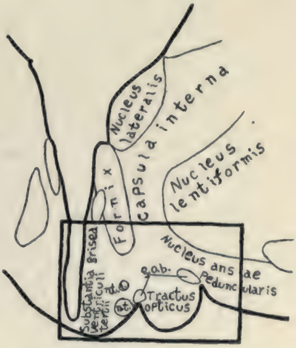


FIG. 14A.

PLATE VIII.

HOMO. SERIES D (CONTINUED).

Magnification of Figs. 15 to 18 = 5 diameters.
Magnification of Figs. 15A to 18A = 2 diameters.

⬤ = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami. }
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.). (Examine with hand lens).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the nucleus ansae peduncularis.
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 17 the closely packed group of cells of the substantia grisea situated just lateral to the ventral tip of the third ventricle (see text).

Note in Fig. 18 the cells of the basal optic ganglion crossing mid line (see text).

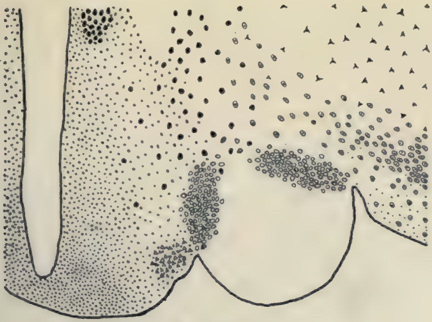


FIG. 15.

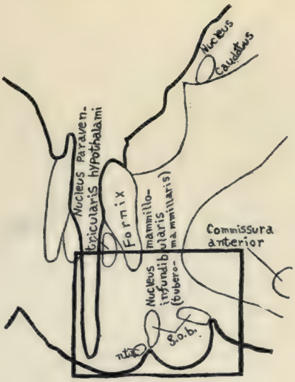


FIG. 15A.

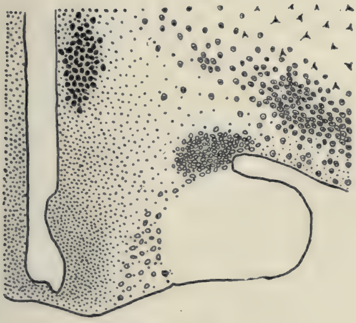


FIG. 16.

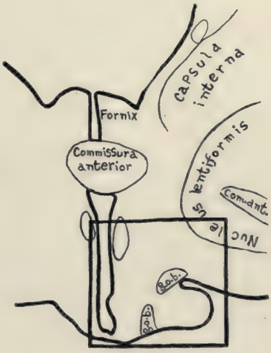


FIG. 16A.

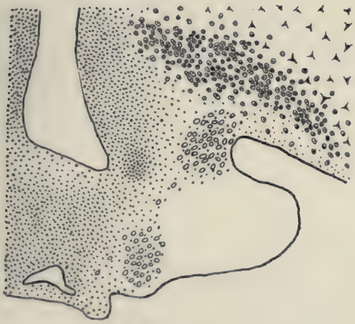


FIG. 17.

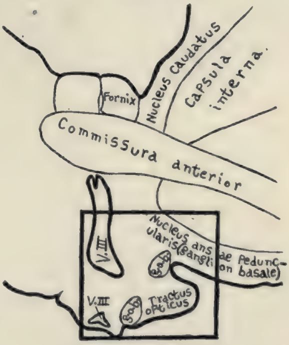


FIG. 17A.

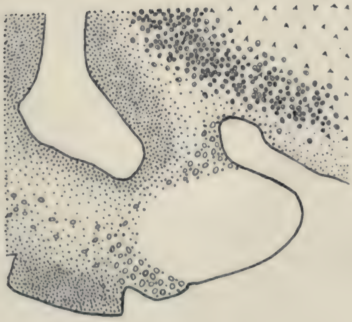


FIG. 18.

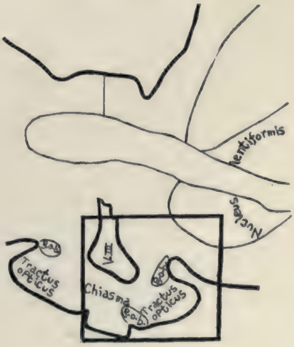


FIG. 18A.

PLATE IX.

MACACUS RHESUS. SERIES A.

Magnification of Figs. 19 to 22 = $6\frac{2}{3}$ diameters.
Magnification of Figs. 19A to 22A = $2\frac{1}{2}$ diameters.
● = Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
• = Cells of the substantia grisea ventriculi tertii.
Δ = Cells of the nuclei tuberis laterales (n. t. l.).
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = { Cells of the corpus hypothalamicum (Luysii).
Cells of the nucleus ansae peduncularis.
° = Cells of the ganglion mediale corporis mammillaris.
▶ = Cells of the nucleus intercalatus corporis mammillaris.
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 22 the group of densely packed cells of the substantia grisea located just lateral to the third ventricle (see text).

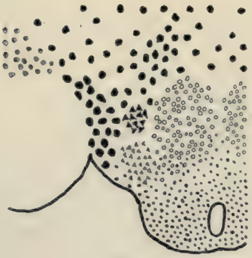


FIG. 19.

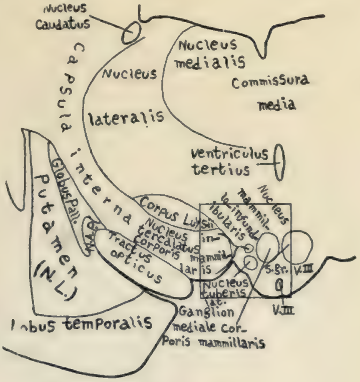


FIG. 19A.

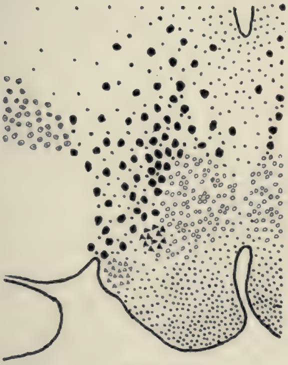


FIG. 20.

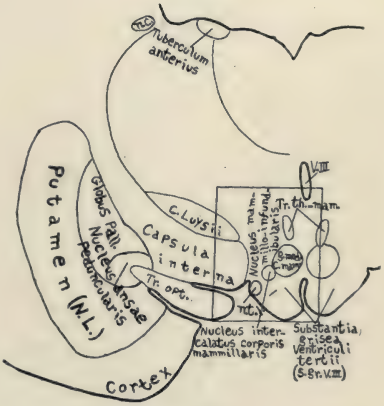

n.c.
Tuberculum anterius
V.III
Putamen (N.L.)
Globus Pall.
Nucleus ansae peduncularis
C. Luysii
Capsula interna
Tr. opt.
Nucleus mammillo-infund-ibularis
Tr. th.-mam.
G.med. C.mam.
nt.
Nucleus intercalatus corporis mammillaris
Substantia grisea ventriculi tertii (S.gr.V.III)
Cortex

FIG. 20A.

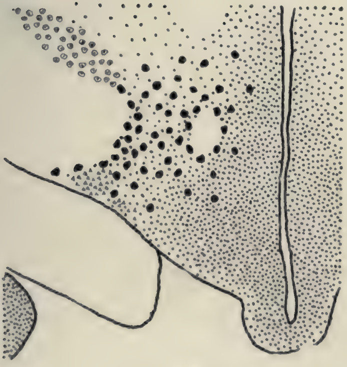


FIG. 21.

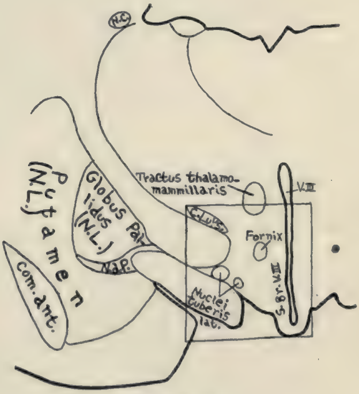


FIG. 21A.

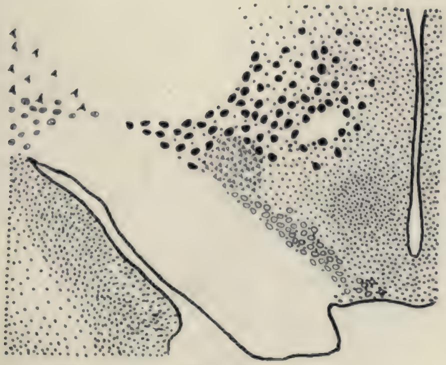


FIG. 22.

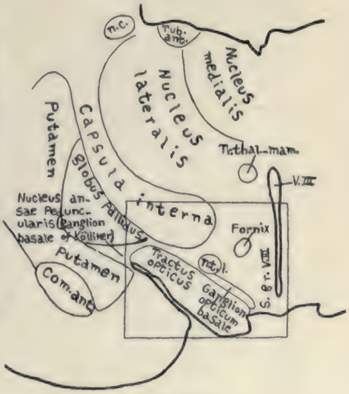


FIG. 22A.

PLATE X.

Macacus Rhesus. Series A (Continued).

Magnification of Figs. 23 to 25 = 6⅔ diameters.
Magnification of Figs. 23A to 25A = 2½ diameters.

$$● = \begin{cases}\text{Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).}\\ \text{Cells of the nucleus paraventricularis hypothalami.}\end{cases}$$

• = Cells of the substantia grisea ventriculi tertii.
○ = Cells of the ganglion opticum basale (g. o. b.).
⊙ = Cells of the nucleus ansae peduncularis (ganglion basale of Kölliker).
. = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 24 lateral from the third ventricle the densely packed group of cells of the substantia grisea; such masses of the substantia grisea should not be confused with the nuclei tuberis laterales.

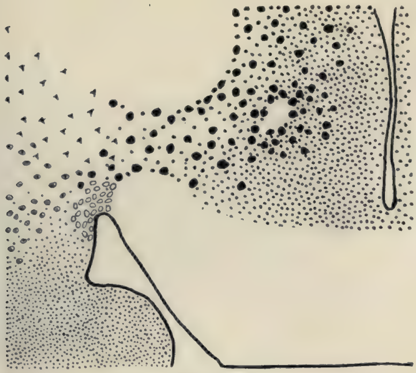


FIG. 23.

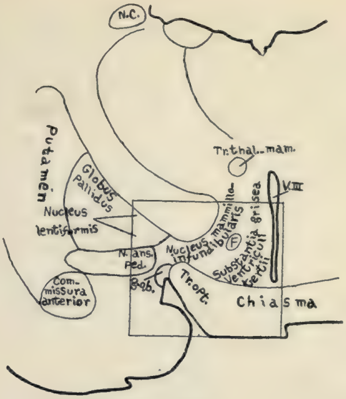


FIG. 23A.

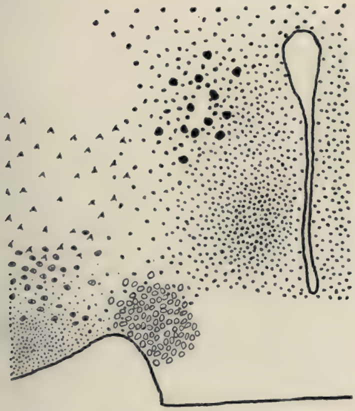


FIG. 24.

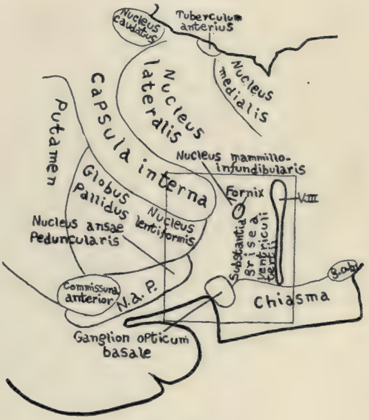


FIG. 24A.

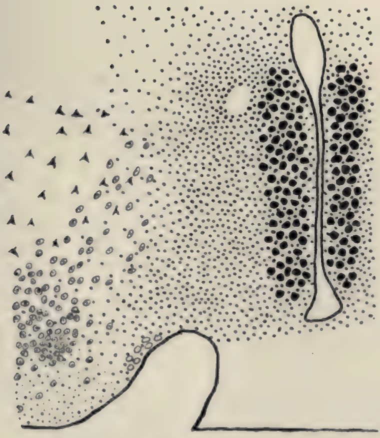


FIG. 25.

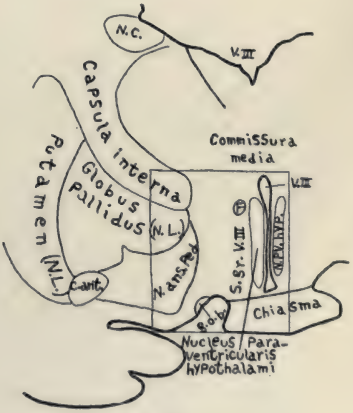


FIG. 25A.

PLATE XI.

LEMUR RUFUS. SERIES A.

Magnification of Figs. 26 to 30 = $8\frac{1}{3}$ diameters.
Magnification of Figs. 26A to 30A = $3\frac{1}{3}$ diameters.

● = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
Cells of the nucleus paraventricularis hypothalami. }
• = Cells of the substantia grisea ventriculi tertii.
○ = Cells of the ganglion opticum basale (g. o. b.).
≻ = Cells of the globus pallidus nuclei lentiformis.

Note in Fig. 27 the absence of the basal optic ganglion (see text).

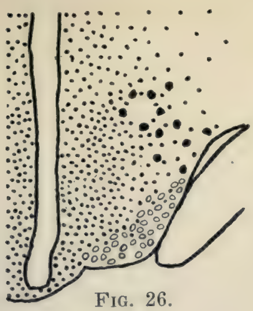


FIG. 26.

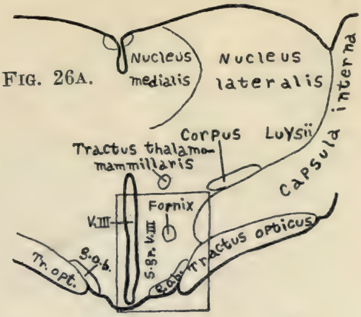


FIG. 26A.

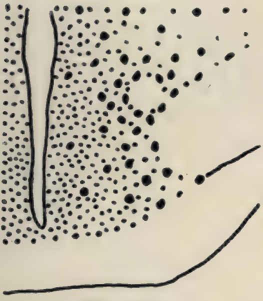


FIG. 27.

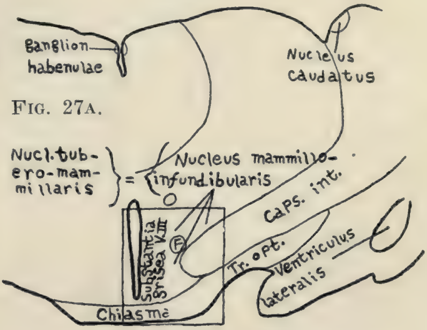


FIG. 27A.

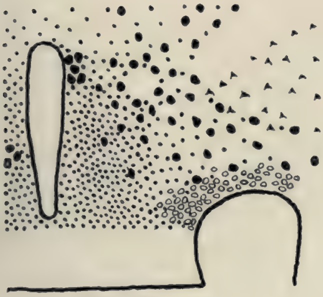


FIG. 28.

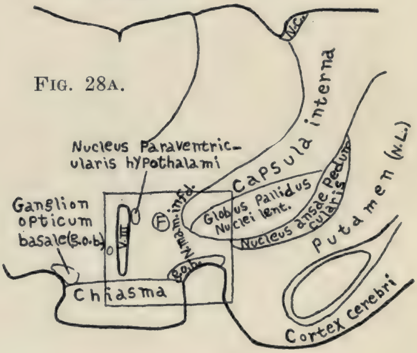


FIG. 28A.

N.C.
Capsula interna
Nucleus Paraventricularis hypothalami
Ganglion opticum basale (g.o.b.)
V.III
F
N. mam. infd.
Globus Pallidus Nuclei lent.
Nucleus ansae peduncularis
Putamen (N.L.)
g.o.b.
Chiasma
Cortex cerebri

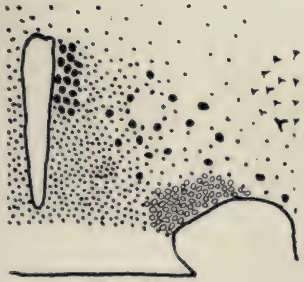


FIG. 29.

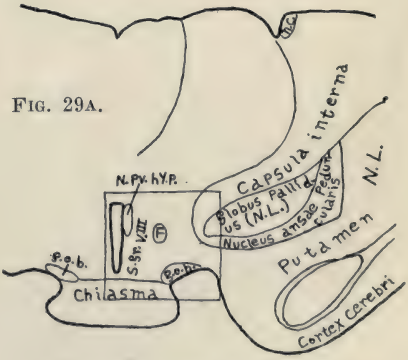


FIG. 29A.

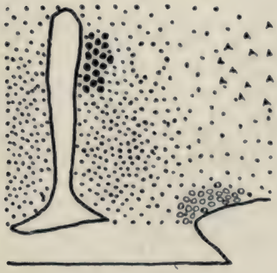


FIG. 30.

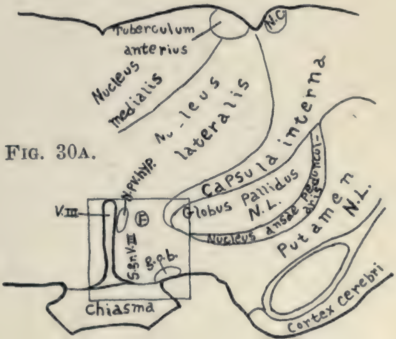


FIG. 30A.

PLATE XII.

CAT. SERIES C.

Magnification of Figs. 31 to 35 = $8\frac{1}{3}$ diameters.
Magnification of Figs. 31A to 35A = $3\frac{1}{3}$ diameters.

● = { Cells of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).
  Cells of the nucleus paraventricularis hypothalami.
• = Cells of the substantia grisea ventriculi tertii.
○ = Cells of the ganglion opticum basale (g. o. b.).
· = Cells of the cortex cerebri.
≻ = Cells of the globus pallidus nuclei lentiformis.

PLATE XII.

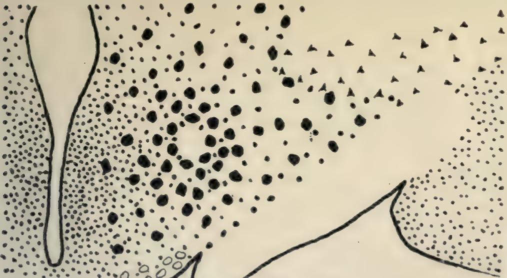


FIG. 31.

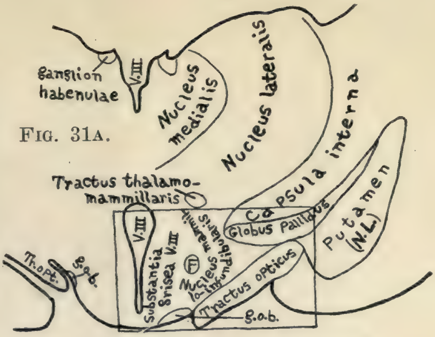


FIG. 31A.

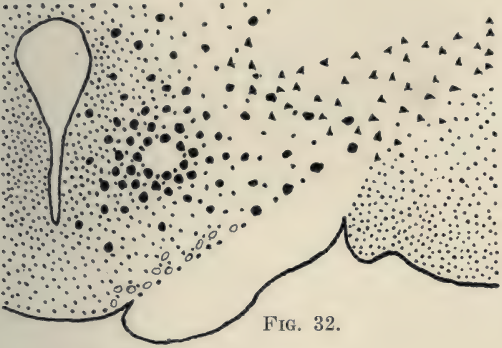


FIG. 32.

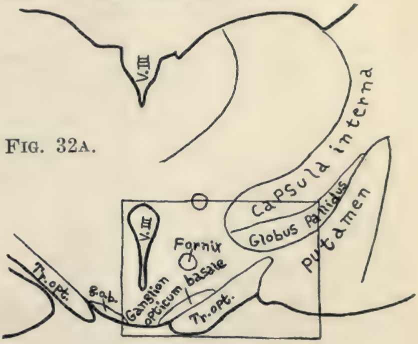


FIG. 32A.

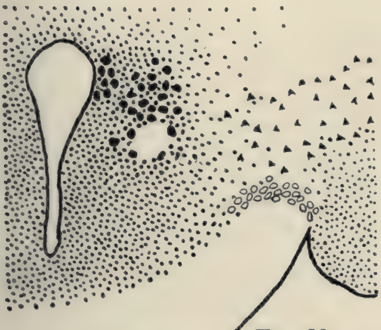


FIG. 33.

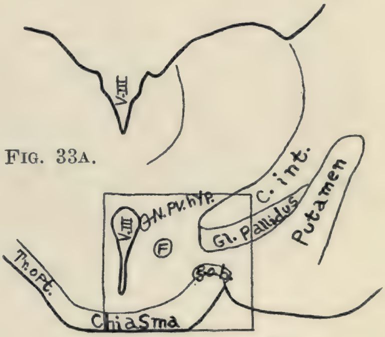


FIG. 33A.

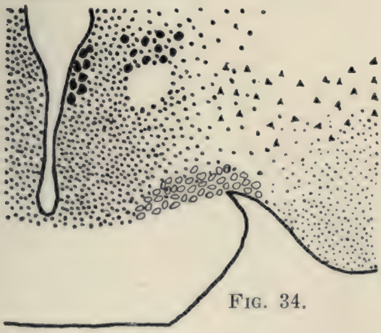


FIG. 34.

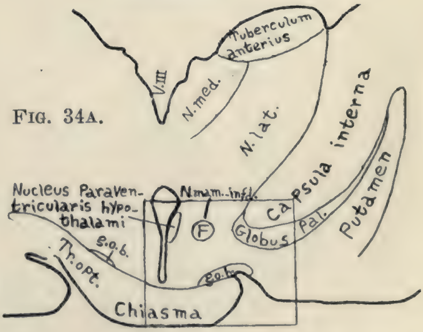


FIG. 34A.

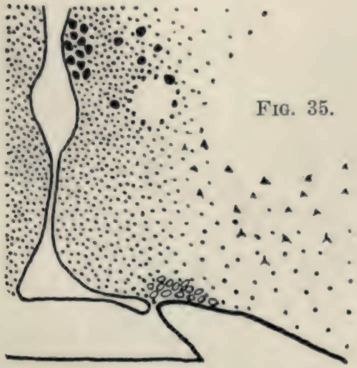


FIG. 35.

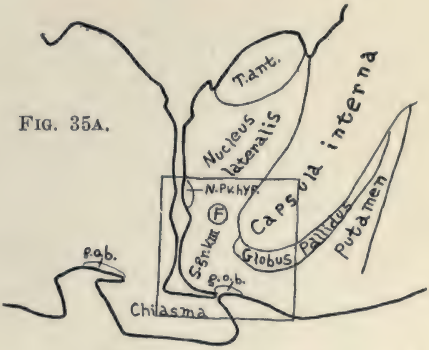


FIG. 35A.

PLATE XIII.

HOMO. SERIES AC. NUCLEI TUBERIS LATERALES.

Fig. 36 represents the actual appearance of a portion of the preparation from which Fig. 4 (Pl. I) was drawn. The preparation was projected at a magnification of 83½ diameters and every cell outlined in pencil. Then under the microscope each cell (as far as this was possible) was identified and reproduced in water color exactly as it appeared. This illustration is accordingly an accurate reproduction of the appearance of the preparation except that bloodvessels and neuroglia have been omitted.

Magnification (after ⅓ reduction) = 55⅔ diameters.

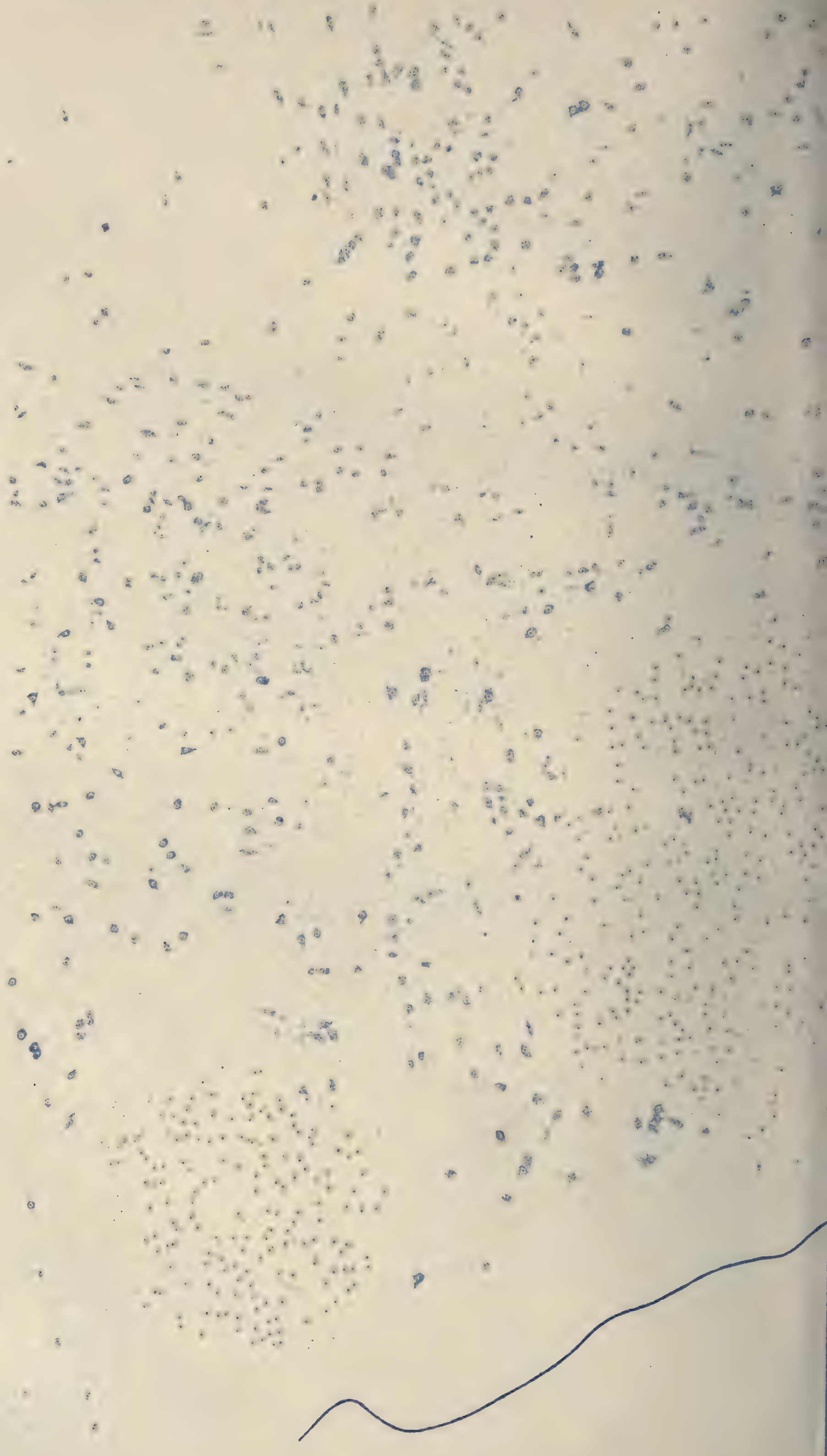
Comparing Fig. 36 with Figs. 4 and 4A it is evident that the region illustrated is the ventro-lateral portion of the tuber cinereum. At the right upper corner is seen a portion of the pes pedunculi, while at the left upper corner appears a portion of the fornix column.

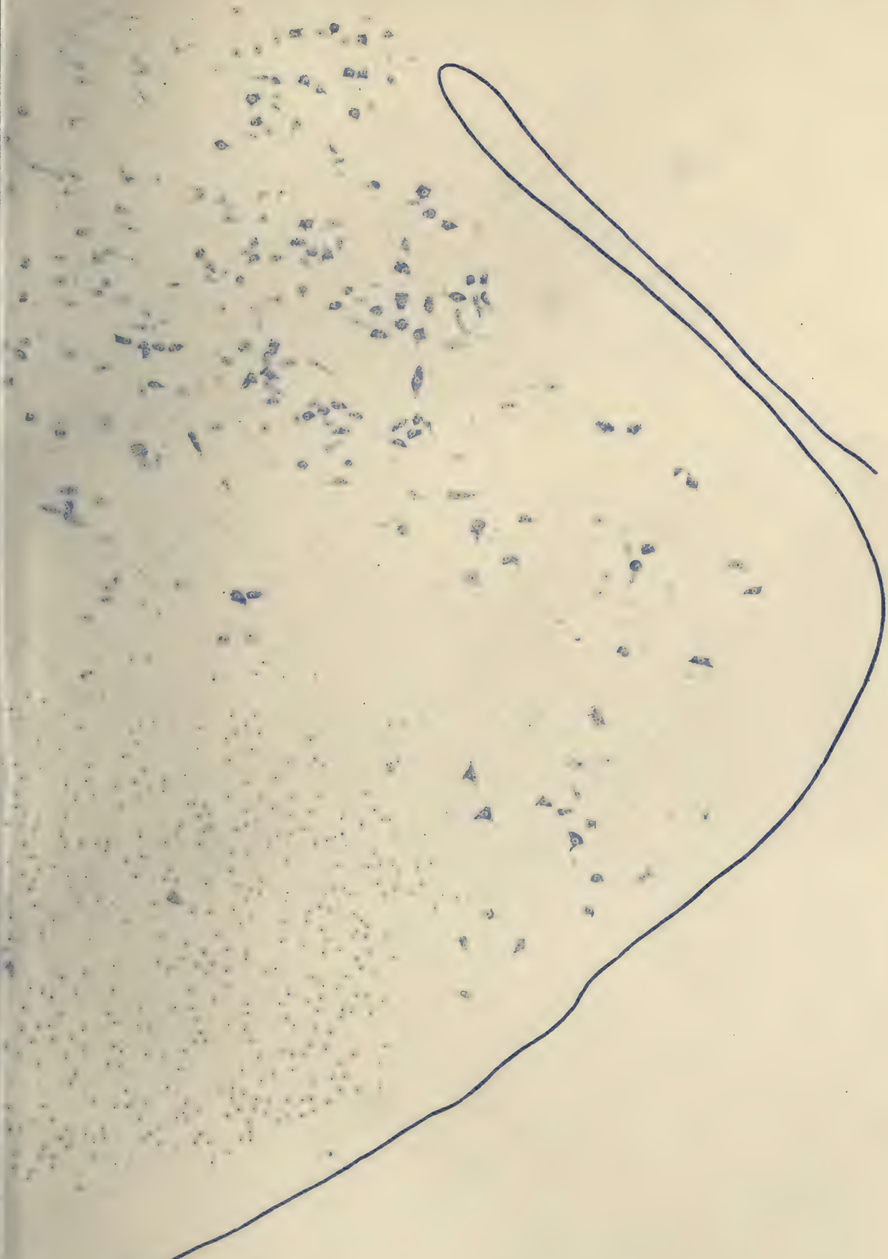
The two groups of small pigmented cells are the nuclei tuberis laterales. Note that they are partly circumscribed by a zone containing few cells.

The large cells are those of the nucleus tubero-mammillaris (nucleus mammillo-infundibularis).

The small pale blue cells are those of the substantia grisea ventriculi tertii. Note transition types between these cells and the large cells of the nucleus tubero-mammillaris; this transition involves both the size of the cells and the intensity of the stain, so that some cells occur which could not be positively assigned to either of these two cell groups.

Compare the various cell groups of Fig. 36 with the corresponding cell types of Pl. XII, where the cells (man) are highly magnified.





36

PLATE XIV.

Homo. Series AC. Ganglion Opticum Basale.

Fig. 37 shows the actual appearance of a portion of the basal optic ganglion in the preparation from which Fig. 9 (Plate III) was drawn. As in the case of Fig. 36 the preparation was projected (but at a magnification of 145 diameters instead of 83½) and every cell outlined in pencil. Then under the microscope every cell (except in rare instances where this was impossible) was identified and reproduced accurately in water color.

Magnification (after ⅓ reduction) = 96⅔ diameters.

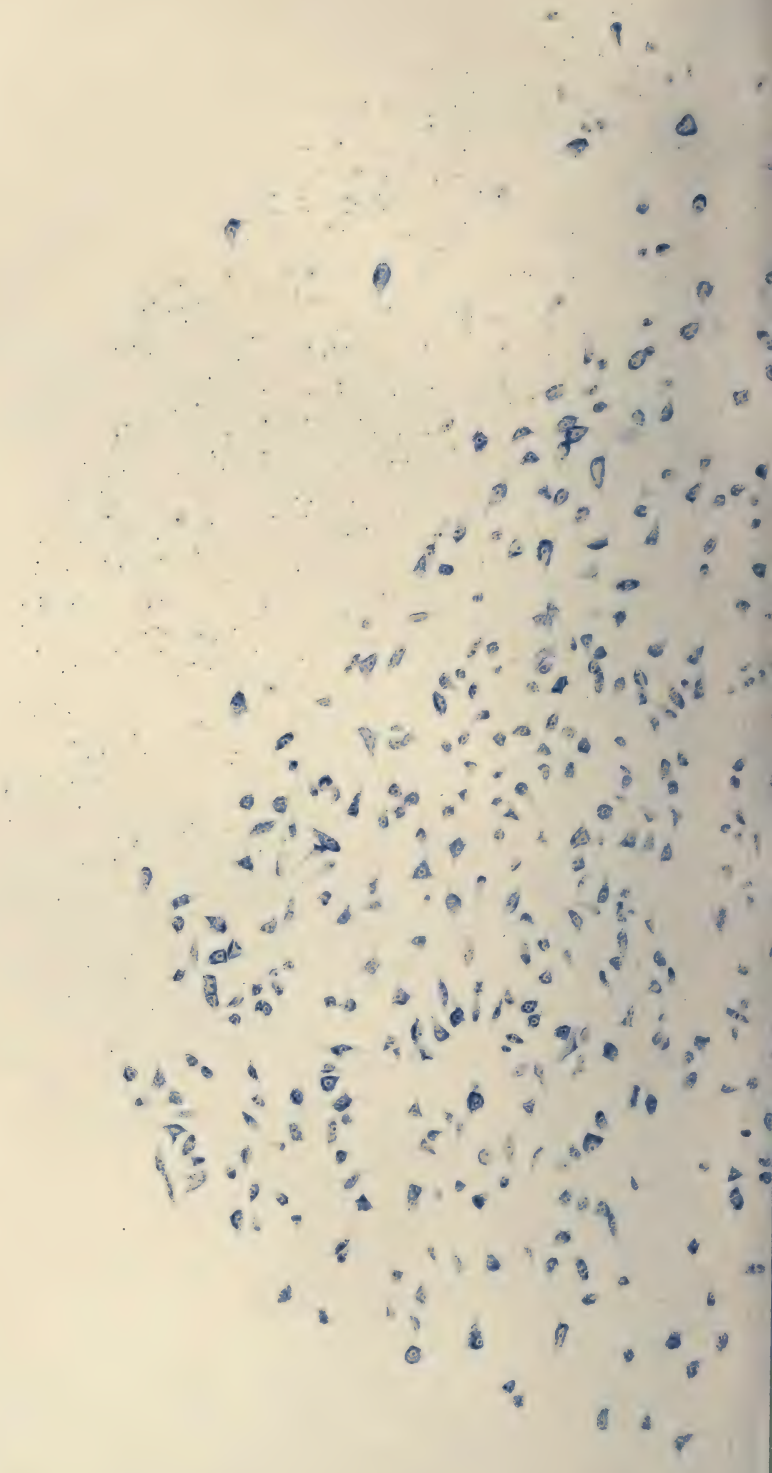
Fig. 37 represents the whole breadth of the basal optic ganglion near its medial pole (Fig. 9, Pl. III), and shows the relation of this nucleus to the substantia grisea of the third ventricle. To the right is seen the ventrolateral surface of the brain (anterior perforated substance).

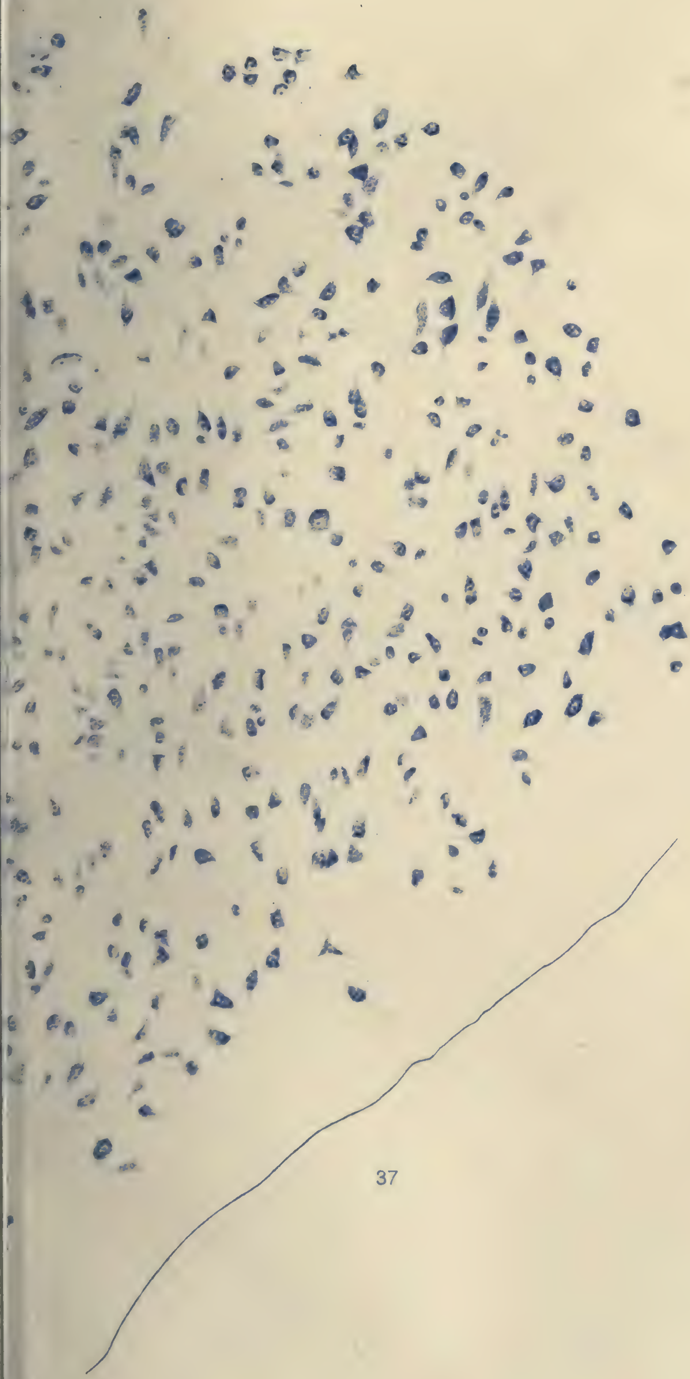
The large deeply staining cells are those of the basal optic ganglion. Note that it is sharply separated from the substantia grisea. The long coarse processes of the cells of the basal optic ganglion are here represented as blue, but in reality they are almost colorless; this figure, however, represents correctly the peculiar appearance of an intercellular feltwork, to which these processes give rise.

The small pale cells are those of the substantia grisea ventriculi tertii. Note the difference in appearance of the intercellular substance from that within the basal optic ganglion, due to the absence of coarse cell processes.

As in Fig. 36 bloodvessels and neuroglia have not been drawn.

See Pl. XII for the appearance of these two cell types (in man) under higher magnification.





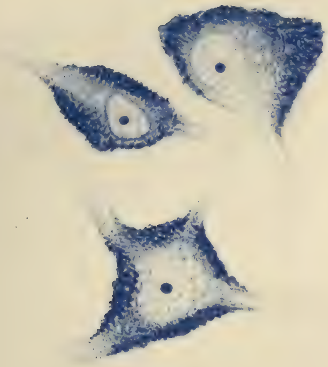
37

PLATE XV.

HOMO. MAGNIFICATION = 580 DIAMETERS.

38. Cells of the ganglion opticum basale.
39. Cells of the nuclei tuberis laterales.
40. Cells of the substantia grisea ventriculi tertii.
41. Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).
42. Cells of the nucleus ansae peduncularis (also known as ganglion basale of Kölliker).
43. Cells of the nucleus paraventricularis hypothalami.

38



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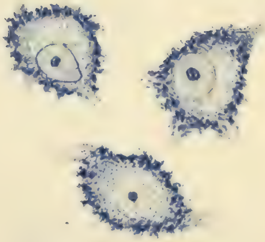

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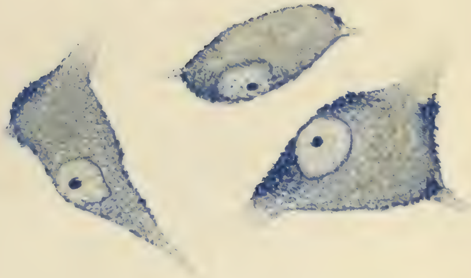

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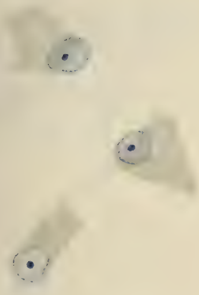

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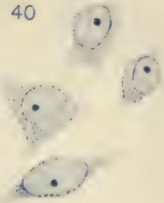

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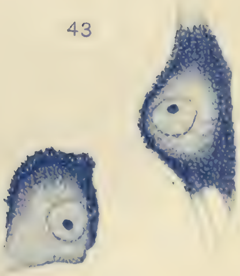
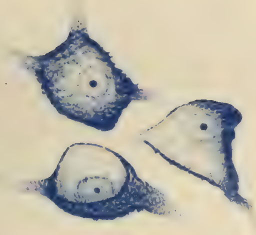


PLATE XVI.

Macacus Rhesus. Magnification = 580 Diameters.

44. Cells of the ganglion opticum basale.
45. Cells of the nuclei tuberis laterales.
46. Cells of the substantia grisea ventriculi tertii.
47. Cells of the nucleus tubero-mammillaris (formerly known as nucleus mammillo-infundibularis).
48. Cells of the nucleus ansae peduncularis (also known as the ganglion basale of Kölliker).
49. Cells of the nucleus paraventricularis hypothalami.

44



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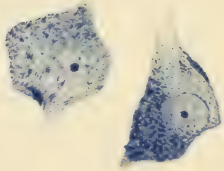

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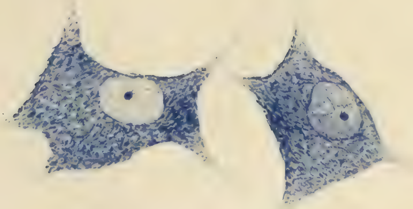

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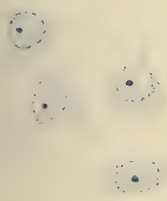

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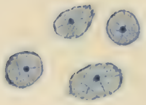

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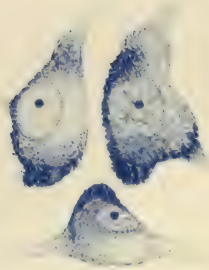
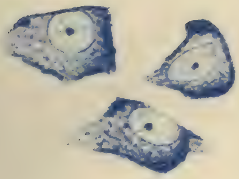


PLATE XVII.

LEMUR RUFUS. MAGNIFICATION = 580 DIAMETERS.

50. Cells of the ganglion opticum basale.
51. Cells of the substantia grisea ventriculi tertii.
52. Cells of the nucleus tubero-mammillaris (formerly known as the nucleus mammillo-infundibularis).
53. Cells of the nucleus ansae peduncularis (also known as the ganglion basale of Kölliker).
54. Cells of the nucleus paraventricularis hypothalami.

50



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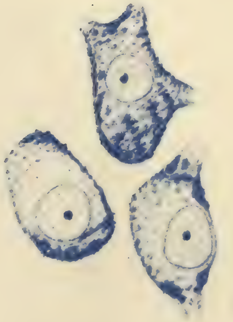

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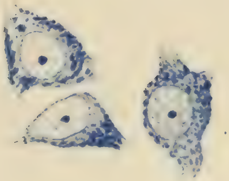

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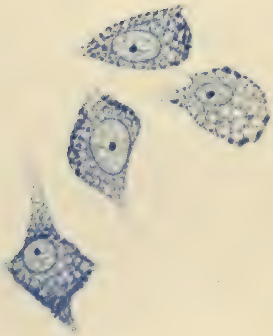

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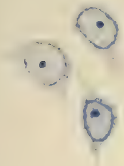
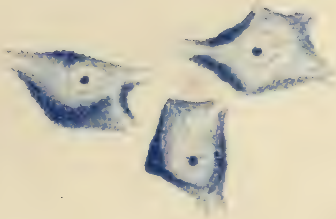


PLATE XVIII.

CAT. MAGNIFICATION = 580 DIAMETERS.

55. Cells of the ganglion opticum basale.
56. Cells of the substantia grisea ventriculi tertii.
57. Cells of the nucleus tubero-mammillaris (formerly known as the nucleus mammillo-infundibularis).
58. Cells of the nucleus paraventricularis hypothalami.

55



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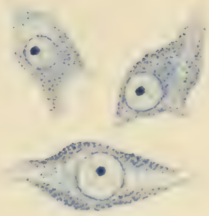

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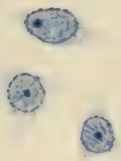

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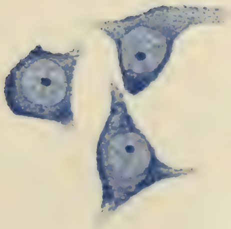

VENOUS THOMBOSIS DURING MYOCARDIAL INSUFFICIENCY.

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Late Resident Physician, The Johns Hopkins Hospital,
AND
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(From the Medical Clinic and the Pathological Laboratory of The Johns Hopkins Hospital.)

Extensive thromboses of venous trunks during a state of insufficiency of the heart muscle, dependent upon valvular disease of the heart or primary myocardial degeneration, have been recognized and reported in a few excellent monographs abroad and in this country. The cases reported, however, are few in number, in fact so few that the condition may be regarded by some as a medical curiosity and as one not deserving careful analysis or attention. This conception should be corrected.

It immediately suggests itself that these thromboses may be readily overlooked, when one bears in mind that they are invariably associated with an extensive cardiac œdema, and that this œdema may not only effectually mask the local circulatory disturbance, *i. e.,* the œdema resulting from thrombosis of a large venous trunk, but also make it impossible to see or palpate the occluded vessel. It is a relatively frequent clinical experience to see an asymmetrical œdema in cases of myocardial insufficiency, and it will be shown that this is not an effect of gravity, as is usually accepted, but much more frequently than supposed is dependent upon an actual venous thrombosis.

The relation of the thrombosis to the outcome of the primary disease is also of importance. The thrombosis itself adds another insult to a constitution already weakened by disease and often though not always leads to death. The outcome is usually directly dependent upon the seriousness of the primary condition. The veins in some cases become canalized, or a sufficient collateral circulation is established to alleviate the mechanical effects of the venous occlusion.

The frequency and importance of the condition have not only been overlooked clinically but very few observations are recorded from the post-mortem table. This may be partly accounted for by the fact that many of the thromboses occurring during myocardial insufficiency are situated in vessels not exposed in the routine autopsy on account of the necessity to avoid mutilation of the body. Many others, located in the large veins, may be very easily dislodged in removal of the heart and then overlooked entirely. This is attested to by the well-known fact that pulmonary emboli are not infrequently missed, unless the operator's attention is especially directed to them by the clinical history, and with this lead the pulmonary vessels are opened *in situ*. It is not particularly uncommon to have one's attention first directed to the possibility of a large pulmonary embolus by finding smaller ones projecting from the larger arterial trunks on section of the lung.

The localization of the thromboses occurring in cases of myocardial insufficiency appears, from the literature, to be most frequently in the veins of the upper extremities. This is of especial interest because it is exceptionally rare to encounter venous thrombi in these vessels in other conditions than the one under consideration. Further, it has been stated repeatedly that the venous trunks of the left side of the body are much more frequently affected than those of the right. This finding has led previous writers to many theories concerning the localization of the thrombosis. Most important among these is the greater length of the left subclavian vein and the possibility that it may be compressed by a dilated auricle. This theory we shall show to be fallacious, since in the analysis of the total number of cases, including those collected from the literature and our own relatively large series, there is practically no difference in the frequency of the thrombosis on the right and the left side.

The type of cardiac lesion with which the accident is reported to occur with greatest frequency is mitral stenosis. It is not unnatural to expect this, since mitral stenosis is, as is well known, one of the most severe of the cardiac affections, leading early in its course to chronic congestion of the systemic vessels. But this is not the only cardiopathy in which extensive venous thrombosis occurs. As will be shown, almost any lesion of the heart resulting in myocardial insufficiency may be associated with thrombosis of the veins of the upper extremities particularly and, more rarely in our experience, of those of the lower, though here too the condition is more frequent than at present imagined.

In the etiology of venous thrombosis the mechanical factor of venous slowing has been emphasized by almost all writers. This slowing is a natural result of the insufficiency of the heart muscle. However, it cannot be the only factor, since it does not account for the relatively greater frequency of the thrombosis in the veins of the upper extremities. To explain this most authors resort to the above mentioned possibility, namely, pressure on the large veins of the left arm by the dilated left atrium. But, as has been pointed out, this cannot be the cause, since thrombosis is no more frequent on the left side than on the right. The abnormal dilatation of the veins themselves has been mentioned by Cohnheim, and it seems reasonable to suppose that their engorgement and dilatation, associated with the slowing of the blood stream, may be of importance in producing retrogressive changes in the vessel walls, which might render them more prone to thrombotic involvement. The most acceptable suggestion concerning the etiology of the thrombosis is that it results from infection. This seems very reasonable and, while still a theoretical possibility, is certainly to be considered. With these etiological factors, slowing of the blood stream, dilatation and engorgement of the venous trunks and infection, all the necessary conditions for thrombosis are present. The localization alone remains unexplained.

Our attention was directed to this subject by the occurrence of what was then thought to be an exceptionally marked instance of venous thrombosis involving all the veins of the right upper extremity together with all of the branches draining into the right innominate vein, even to its finest ramifications. This was associated with a myocardial insufficiency resulting from a severe primary myocarditis.

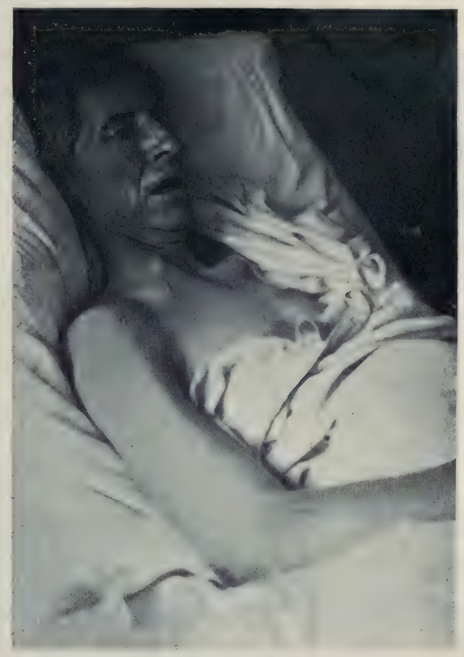
The following is a brief account of the case with photographs:

J. H. H. Serial No. 59.—R. F. W., male, white, aged 49 years. *Clinical diagnosis:* Myocardial insufficiency; thrombosis of right innominate, jugular and subclavian veins and their branches; pulmonary infarction. Death. Autopsy.

The past history was unimportant. The onset of the terminal illness was four months before admission with cough and dyspnœa. For three weeks patient remained in a state of myocardial insufficiency with cyanosis, dyspnœa, œdema of the lungs, rapid and irregular pulse, an enlarged heart without murmurs and an enlarged and tender liver.

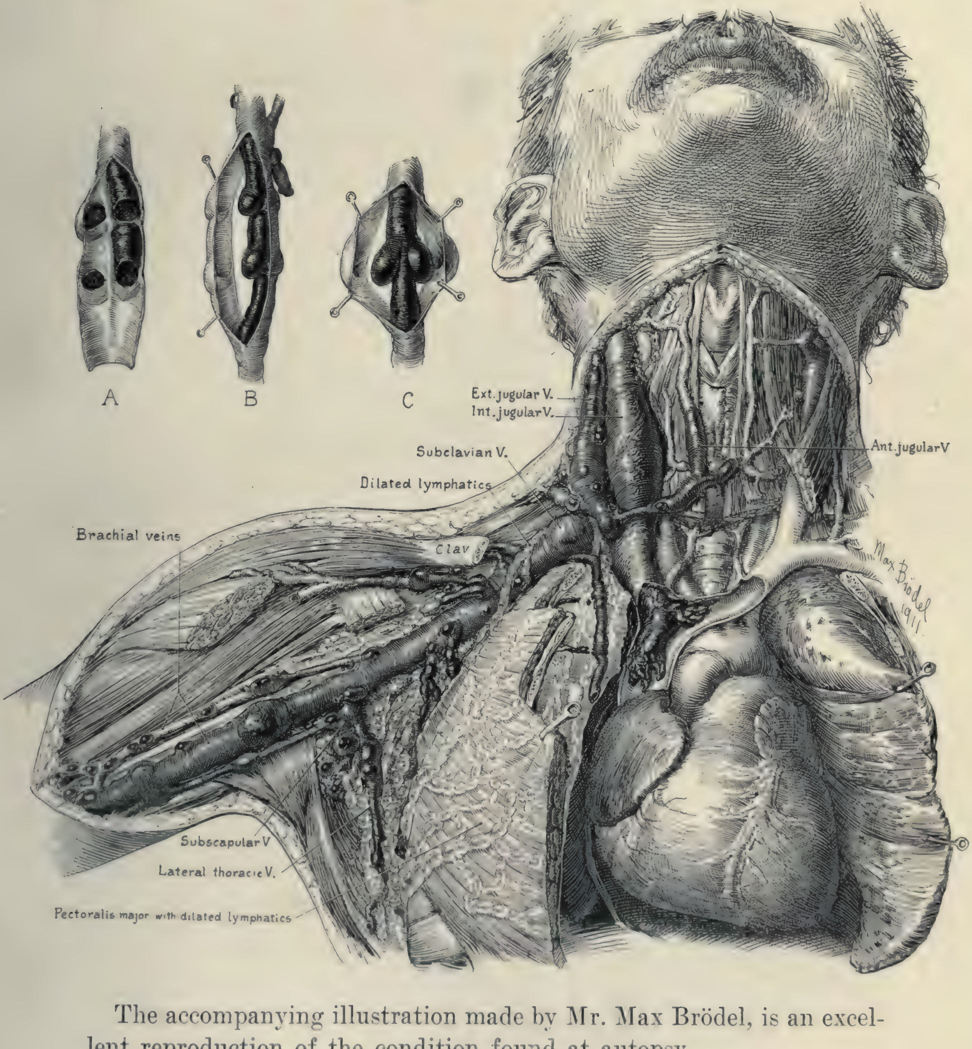
Two days before death swelling of the right arm was noticed and regarded as a mechanical effect of gravity in the general anasarca. It increased the next day, and thick, firm whip-cords could be traced from elbow to axilla in the course of the brachial vein. The right external jugular stood out prominently. Before death small thrombosed veins were apparent in the right pectoral region and in the region of the thyroid gland. Blood cultures and cultures from the thrombosed veins *intra vitam* remained sterile. Fever and leucocytosis were present.

Anatomical diagnosis: Chronic fibrous myocarditis; dilatation and hypertrophy of the heart; cardiac insufficiency; chronic passive congestion of the viscera; multiple mural puriform thrombi of right and left ventricle; healed and healing anæmic infarcts of spleen and kidneys; thrombosis of right superior vena cava; propagated thrombus extending into the large veins of the neck and right arm; œdema of right arm; multiple pulmonary emboli with multiple hæmorrhagic infarcts of the lungs; acute pleuritis (right); hemorrhagic exudate; chronic splenic tumor; chronic perisplenitis; fatty degeneration of liver; chronic fibrous epididymitis; thrombi in the spermatic and prostatic veins.



PHOTOGRAPH ON SECOND DAY OF THROMBOSIS SHOWING PROMINENT JUGULAR VEINS AND ŒDEMA OF THE RIGHT ARM.

The right portion of the thorax and the right arm are very œdematous. The arm measures half again the circumference of the left arm. In the upper portion of the anterior mediastinum the veins stand out as large firm cords. The right innominate vein and all of its neck and arm branches are similarly involved. Along the course of the veins bulbous nodules protrude, which show the situation of the valves within. The entire subcutaneous tissue in the region where these veins are thrombosed is very markedly œdematous, and on section one sees that this œdema is partly interstitial, but partly due to a tremendous dilatation of the lymphatics, some of which in the region of the lymphatic duct and along the course of the subclavian vein and in the axilla are almost 1 cm. in diameter. They contain a clear, yellowish fluid.



The accompanying illustration made by Mr. Max Brödel, is an excellent reproduction of the condition found at autopsy.

During the year 1913, while reviewing the 49 cases in the literature, five examples of venous thrombosis during myocardial insufficiency were observed in this clinic. This suggests strongly that it occurs much more frequently than has been supposed.

In the following paper the literature will first be reviewed, and then the 48 reported cases, with our own 17 cases, will be presented. We shall attempt to correlate the clinical and pathological pictures and the cases will be analyzed with this point in view.

LITERATURE.

In 1845 Bouchet reported the first case in the literature of venous thrombosis during myocardial insufficiency. He, like many subsequent writers, failed to appreciate the importance of their simultaneous occurrence.

Peter (1873), one of the first to become interested in the etiology of thrombosis in this condition, believed the cachexia of cardiopathies was the essential factor in producing thrombosis; it was a popular theory that the blood was changed to a hyperinotic condition and the tendency to coagulation thereby increased.

The anatomical peculiarities of the venous trunks of the upper extremities impressed Hanot. In 1874, he pointed out that the left brachiocephalic trunk was longer and more oblique than the right, making the return of the blood from the left side more difficult than from the right, even in a normal person. This he thought to be supported by the fact that cardiac œdema appears earlier and persists longer in the left upper extremity.

Parmentier (1889) further emphasized what Hanot had pointed out. He believed that while ordinarily the stream would be slower in the longer, more oblique veins from the left side, a condition of insufficient heart muscle would accentuate the relative venous stagnation.

More extensive consideration of the subject is found in Hirschlaff's Inaugural Dissertation (1893) "Upon the Causes of Thrombosis in the Upper Extremities." In a series of 20 cases he contrasted two that had occurred during myocardial insufficiency with 18 complicating aneurysm, malignant disease, tuberculosis, pneumonia and acute infections. Hirschlaff explains the localization of the thrombosis in myocardial insufficiency as follows: He believed that unusual dilatation of the venous trunks and consequent slowing of venous flow were not the only factors, although conspicuous ones. The endothelial defects of the vessel wall or areas of endophlebitis, emphasized by Cohnheim, Hirschlaff considered to be small and difficult to locate.

He pointed out that the valves on the left side at the junction of the subclavian and internal jugular veins are more often insufficient than those on the right. This led him to conclude that there was a relation between the thrombosis and the insufficiency of the venous bulb valves accounting for the more frequent occurrence of the thromboses on the left side. He believed also in the importance of the greater length of the veins on this side and that they emptied themselves with greater difficulty. This he thought manifested itself clinically in the earlier occurrence of œdema in the left arm in developing anasarca. The localization of the thrombosis at the junction of the subclavian and jugular veins, Hirschlaff thought might be due to many causes. First, platelets tend to accumulate at places where veins meet (Ebert and Schimmelbusch) and here, where the large valves of the veins are located and where two large veins meet at a sharp angle, the eddy (*Wirbelbewegung* of v. Recklinghausen) is marked and may promote clotting. Further, he ingeniously suggests the emptying of infectious material from the thoracic duct into the subclavian vein at this location as a possible factor in the localization of the thrombosis.

The first communication in the English literature was by Baldwin (1897), who collected 34 cases of jugular thrombosis. Only one of these, however, developed during myocardial insufficiency. To Baldwin the etiological factors were: (1) The sluggish or arrested circulation; (2) an infectious process in the vein, that is, an injury due to bacterial invasion of the blood; (3) a morbid condition of the blood rendering it more coagulable.

Poynton (1898) stated that the process occurred where the vertical jugular current meets the cross current from the subclavian vein. The frequency of active carditis suggested to him that the thrombosis might be associated with a similar infectious process in the veins.

Gallavardin reviewed the cases in the literature up to 1900. He noted the frequent association of the thrombosis with mitral stenosis and the fact that it occurred most frequently in the veins of the upper extremity, especially in those of the the left side. He emphasized the occurrence of the thrombosis during cardiac decompensation and the constant fatality of the affection. Cachexia and stasis appealed to him as causative factors of the thrombosis, and he considered that bacteria must be accepted as the cause of the clotting. He says in conclusion: "This venous thrombosis in heart cases forms a distinct group, possessing etiological, anatomical and clinical individuality, unique especially in their causation, localization and fate."

This brings us to the best and most comprehensive consideration of the subject, the monograph by Welch * in 1900. He reported five cases of his own and 23 from the literature.

Welch states: "In the great majority of cases the thrombosis appeared during a condition of failure, generally extreme failure, of compensation of advanced mitral disease." In 24 of the 28 cases the thrombi were found in the veins of the neck and arms and so constitute a special group of thromboses of the upper extremity. This group of thromboses was associated almost exclusively with mitral disease, stenosis leading. This suggested to Welch that a dilated left auricle or dilated pulmonary vessels may press upon the left subclavian vein, and play a part in determining the localization of the thrombi. Additional factors he believed to be the valves of the veins, the bulbous jugular base, the attachment of the veins to the fascia, the coming together at oblique or right angles of venous currents at different speeds, and the systolic reflux in tricuspid insuffiency. In conclusion, he emphasized as the cause of the thrombosis and its localization: (1) The particular disturbance of the circulation; (2) the anatomical structure and disposition of the veins; (3) infection as the most probable etiological factor.

Huchard collected 50 cases in 1905 and gave the subject very complete consideration. He, too, emphasized the rôle of infection and cited the concurrent presence of fever, bronchitis, pleurisy, pneumonia, etc., as further evidence of this point. He pointed out that, clinically, jugular-subclavian thrombosis has an onset with pain followed by swelling of the face, neck and upper extremity. The œdema becomes hard and cyanotic. In the neck it resembles parotitis (Cheadle and Lees). It spreads over the thoracic wall and involves the mammary gland (Hanot). There is pain in the course of the vein. Hard cords are palpable and visible.

Finally, Blumer noted that canalization or collateral circulation, sufficient to carry off the blood, may occur, but may be entirely insufficient under the stress of the serious decompensation.

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* Welch's paper "Venous Thrombosis as a Complication of Cardiac Disease" includes cases not necessarily in a state of myocardial insufficiency, the criterion of the writers. Some of these, therefore, have been excluded from our series.

REPORT OF CASES.

The following is a very brief digest of the cases found in the literature, arranged in chronological order.

No mention is made of the dyspnœa, cyanosis, cough and bloody expectoration, abdominal pain and such manifestations of the varying degrees and combinations of pulmonary œdema, passive congestion of the liver and viscera, ascites and effusions in other serous sacs, and œdema, indicative of myocardial insufficiency. Every case supplies this picture to a greater or lesser extent. Where possible the sex, age, etiology of the cardiac affection, the cardiac lesion, symptoms and signs of thrombosis, localization of thrombosis, result, duration of observation, autopsy, conformation and additional important autopsy findings will be given.

No. 1.—Bouchet (Gaz. méd. de Par., 1845, xiii, 2^me^ s. 245): Male, age (?). Myocardial insufficiency. Cyanosis, œdema of face, neck and arms. Palpable painful, firm veins. Collateral circulation over chest. Thrombosis of superior vena cava, jugulars and axillaries of both sides and their branches. Recovery in five months.

No. 2.—Cohn (Klinik der embolischen Gefässkrankheiten, Berl., 1860, S. 118): Female, aged 61 years. Marked arteriosclerosis and hemiplegia four years before present illness. Aortic stenosis and insufficiency. Œdema of left foot and leg. Fourteen weeks later œdema of right leg. Thrombosis of both iliac veins. Death in 14 weeks. Autopsy.

No. 3.—Ramirez (Gaz. méd. de Par., 1867, xii, 716): Male, aged 12 years. History of acute rheumatic fever one year before present illness. Aortic and mitral insufficiency. Painful œdema of right and left arms during general anasarca. Thrombosis of right jugular, axillary, subclavian veins and branches. Death in 24 hours. No autopsy.

No. 4.—Ramirez (Gaz. méd. de Par., 1867, xii, 716): Male, aged 50 years. Aortic and mitral insufficiency. Aortic stenosis. Painful, hard œdema of left neck and arm. Palpable cords. Thrombosis of left jugular and subclavian veins and branches. Death in two days. Autopsy.

No. 5.—Diuguet (Thèse de Par., 1872): Sex (?) Age(?) Mitral stenosis and insufficiency, rheumatic in origin. Painful hard œdema of left arm with palpable axillary veins. Thrombosis of left subclavian, axillary and brachial veins. Autopsy: Pulmonary infarcts.

No. 6.—Audral (Bull. Soc. anat. de Par., 1873, xlviii, 328): Old woman. History of two attacks of acute rheumatic fever at nine. Mitral stenosis and insufficiency. Painful œdema of left neck and arm. Evidence of collateral circulation. Thrombosis of left subclavian, jugular and axillary veins. Death. Autopsy: Pulmonary infarcts.

No. 7.—Peter (Leçons de clinique méd., 1873, i, 209): Woman. Age (?) Mitral stenosis and insufficiency. Painful œdema of left arm. Later œdema and tenderness in left neck. Hard, palpable veins. Recovery in three weeks.

No. 8.—Hanot (Compt. rend. Soc. de biol., 1874, i, 80): Female, aged 58 years. Mitral stenosis and insufficiency. Œdema of left arm. One month later, œdema of right arm. Thrombosis of left and right subclavian veins. Death in six months. No autopsy.

No. 9.—Hanot (Compt. rend. Soc. de biol., 1874, i, 80): Female, aged 40 years. Endocarditis of aortic and mitral valves. Œdema of left arm. Thrombosis of left subclavian vein. Death in three months. No autopsy.

No. 10.—Hanot (Compt. rend. Soc. de biol., 1874, i, 80): Female, aged 57 years. Aortic insufficiency and stenosis. Œdema of left arm. Thrombosis of left subclavian vein. Death in four weeks. No autopsy.

No. 11.—Hanot (Compt. rend. Soc. de biol., 1874, i, 80): Male, aged 73 years. Mitral insufficiency. Œdema of left arm. Thrombosis of left subclavian vein. Death in one month. No autopsy.

No. 12.—Dreyfus (Bull. Soc. anat. de Par., 1875, l, 599): Female, aged 37 years. History of acute rheumatic fever at 20. Mitral stenosis and insufficiency, and aortic insufficiency. Painless œdema of left arm. Thrombosis of left subclavian vein. Jaundice. Acute endocarditis. Renal infarction. Death in one month. Autopsy: Pulmonary infarcts.

No. 13.—Robert (Bull. Soc. anat. de Par., 1880, lv, 314): Female, aged 30 years. History of cardiac symptoms following pneumonia eight years before present illness. Mitral stenosis. Œdema of left arm and left face. Palpable veins in left neck. Collateral circulation. Thrombosis of left innominate, subclavian, and jugular veins. Death in one month. Autopsy: Pulmonary infarcts.

No. 14.—Malibran (Bull. Soc. anat. de Par., 1884, lix, 104): Female, aged 49 years. Mitral stenosis and insufficiency. Pain in left groin and popliteal space. Hard, firm cord. Painful œdema of left leg. Thrombosis of left femoral and popliteal veins. Death in 47 days. Autopsy.

No. 15.—Potherat (Bull. Soc. anat. de Par., 1889, lxii, 620): Male, aged 40 years. Aortic insufficiency, not recognized clinically. General œdema including face and arms. Thrombosis of right subclavian and jugular veins. Death in two days. Autopsy: Pulmonary infarction.

No. 16.—Parmentier (Arch. gén. de méd., 1889, ii, 91): Female, aged 40 years. Mitral insufficiency, probably following puerperal infection four years before present illness. Painful œdema of left arm and breast. Thrombosis of left subclavian vein. Jaundice and fever. Death in four days. Autopsy.

No. 17.—Ormerod (Trans. Path. Soc. Lond., 1889, xl, 75): Sex ? Age ? Mitral stenosis. Œdema of right arm, later of left arm. Thrombosis of both innominate, jugular and subclavian veins. Death. Autopsy.

No. 18.—Hirschlaff (Inaug. Diss., Berl., 1893): Female, aged 53 years. History of acute rheumatic fever at 12, 15, 18, 20 and 22. Mitral insufficiency and stenosis, and aortic insufficiency. Œdema of both hands, left half of thorax, left supraclavicular fossa and left face. Disappearance of pulse in left external jugular vein. Painful hard jugular cord. Thrombosis of left innominate subclavian, and jugular veins. Jaundice. Death in six days. Autopsy.

No. 19.—Hirschlaff (Inaug. Diss., Berl., 1893): Female, aged 51 years. History of acute rheumatic fever at 20. Mitral stenosis, aortic insufficiency, tricuspid stenosis. Painful swelling of left neck and arm. Three weeks later swelling of right neck and face and over right thorax. Thrombosis of superior vena cava, left innominate vein and branches. Jaundice. Death in one month. Autopsy: Pulmonary infarcts and fresh endocarditis.

No. 20.—Huchard (Le Bull. méd., 1894, viii, 423): Female, aged 24 years. History of two attacks of acute rheumatic fever seven years before last illness. Mitral stenosis. Painful œdema of left arm. Thrombosis of left brachial vein. Death in 10 days. Autopsy: Pulmonary infarction.

No. 21.—Gatoy (Thèse, de Par., 1895): Female, aged 25 years. History of acute rheumatic fever 20 years before last illness. Mitral stenosis and insufficiency. Hard œdema of left arm and hard brachial cord. Thrombosis of left brachial vein. Chills. Death. Autopsy: Pulmonary infarcts.

No. 22.—Meslay (Rev. mens. d. mal. de l' enf., 1895, xiii, 559): Female, aged 13 years. History of two attacks of acute rheumatic fever one year before final illness. Mitral stenosis and insufficiency. Adherent pericardium. Pain and swelling in right arm involving neck next day. Palpable cords. Thrombosis of right innominate, subclavian and jugular veins. Fever. Enlarged axillary and cervical glands. Death in 16 days. Autopsy: Pulmonary infarcts.

No. 23.—Mader (Jahrb. d. Wien. K. K. Krankenanst., 1895, iv, 252): Female, aged 45 years. History of acute rheumatic fever. Mitral stenosis and insufficiency. Pain and swelling of arms, neck and upper chest. Collateral circulation to epigastric veins. Thrombosis of both innominate veins. Recovery.

No. 24.—Kahn (Arch. gén. de méd., 1896, vi, 469): Female, aged 52 years. Mitral insufficiency. Painless œdema of right hand, arm and breast. Thrombosis of right subclavian vein. Fever. Chronic lymphadenitis about subclavian vein. Death in 20 days. Autopsy: Pulmonary infarcts; pneumococcus isolated from the thrombus.

No. 25.—Baldwin (J. Am. M. Asso., 1897, xxix, 371): Female, aged 19 years. History of five attacks of acute rheumatic fever seven years before present illness. Aortic, mitral and tricuspid stenosis and insufficiency. Pain and swelling of left axilla and neck. Tender tortuous cords. Thrombosis of left innominate, jugular and subclavian veins. Death in nine days. Autopsy: Pulmonary infarcts.

No. 26.—Nicolle et Robineau (La Normandie méd., 1897, xii, 68): Female, aged 16 years. History of repeated attacks of acute rheumatic fever four years before final illness. Mitral stenosis and insufficiency. Pain and œdema of left neck and head. Painful palpable jugular cord, followed in 10 days by œdema of left arm. Thrombosis of left innominate, jugular and subclavian veins. Jaundice. Death in 23 days. Autopsy: Pulmonary infarcts; chronic lymphadenitis about subclavian vein.

No. 27.—Poynton (Lancet, Lond., 1898, ii, 206): Female, aged 19 years. History of acute rheumatic fever nine months before final illness. Aortic and mitral insufficiency and adherent pericardium. Swelling of left arm, face, right arm and chest. Thrombosis of superior vena cava, both innominate veins and branches. Jaundice. Death in two weeks. Autopsy.

No. 28.—Poynton (Lancet, Lond., 1898, ii, 206): Female, aged 21 years. History of acute rheumatic fever as a child and also two years before final illness. Mitral insufficiency. Œdema of left face. Thrombosis of left jugular vein to angle of jaw. Fever, sweats and jaundice. Death in three days. Autopsy: Pulmonary infarcts; fresh endocarditis.

No. 29.—Poynton (Lancet, Lond., 1898, ii, 206): Female, aged 9 years. Mitral insufficiency. Œdema of face, neck, arms and chest. Palpable jugular cords. Thrombosis of superior vena cava, both innominate veins and branches. Death in eight days. Autopsy: Fresh endocarditis; negative cultures from blood.

No. 30.—Gallavardin (Province méd., 1899, xxxv, 409): Female, aged 16. History of chorea at seven. Mitral insufficiency and stenosis. Firm, painful swelling of left arm and neck. Palpable cords. Thrombosis of left subclavian and jugular veins. Death in two days. Autopsy: Pulmonary infarcts.

No. 31.—Gallavardin (Province méd., 1899, xxxv, 409): Female, aged 30 years. Mitral stenosis. Swelling in neck above right clavicle. Pain along right jugular veins. Jugular cord. Thrombosis of right jugular vein. Recovery in one month.

No. 32.—Hanot (Arch. gén. de méd., 1899, 91): Female, aged 40 years. Mitral insufficiency. Œdema of left arm and breast. Thrombosis of left subclavian vein. Death. Autopsy.

No. 33.—Gallavardin (Lyon méd., 1900, xci, 10): Female, aged 53 years. History of heart trouble for two years. Mitral insufficiency and stenosis. Pain below left clavicle. Swelling of left hand and arm. Collateral circulation. Red, painful swelling of right leg for two months. Thrombosis of left subclavian, jugular and right femoral veins. Recovery.

No. 34.—Kinnicutt (Trans. Assn. Am. Phys., 1900, xv, 469): Male, aged 58 years. Mitral stenosis and insufficiency. Pain and œdema of left arm, neck and face. Collateral circulation. Thrombosis of left jugular and subclavian veins. Recovery.

No. 35.—Biggs (Trans. Assn. Am. Phys., 1900, xv, 469): Female, aged 20 years. Mitral insufficiency. Pain and œdema of left arm, neck and chest. Thrombosis of left innominate, jugular and subclavian veins. Death in four weeks. Autopsy: Enlarged glands about jugular vein.

No. 36.—Ford (Phila. M. J., 1900, vi, 960): Male, aged 56 years. History of acute rheumatic fever as a child. Mitral insufficiency and stenosis. Tender, hard mass in right groin and popliteal space. Thrombosis of right common iliac vein. Death in one month. Autopsy.

No. 37.—Macgregor (Amer. Med., 1901, i, 353): Male, aged 46 years. Mitral stenosis. Cyanotic, painful swelling of left arm and neck. Collateral circulation. Thrombosis of left jugular and subclavian veins. Death in six weeks. No autopsy.

No. 38.—White (Clin. J., 1902, xx, 297): Female, aged 24 years. History of acute rheumatic fever and tonsillitis. Mitral and aortic insufficiency and stenosis. Tender swelling of left neck, shoulder and arm. Jugular cords on both sides. Thrombosis of left subclavian and jugular veins and right jugular vein. Recovery in three and one-half months.

No. 39.—White (Clin. J., 1902, xx, 297): Male, aged 26 years. Mitral insufficiency. Hard, palpable jugular veins. Thrombosis of right and left jugular veins. Recovery.

No. 40.—Favier (Thèse de Lyon, 1903): Female, aged 60 years. Myocardial degeneration. Painful, swollen left jugular vein. Jugular cord. Exophthalmos. Right hand swollen. Collateral circulation. Thrombosis of left jugular and right brachial veins. Death. No autopsy.

No. 41.—Favier (Thèse de Lyon, 1903): Female, aged 36 years. History of acute rheumatic fever at 20. Myocarditis. Cyanotic, painful swelling of right arm. Palpable axillary and jugular cords. Axillary adenitis. Torticollis. Collateral circulation. Thrombosis of right subclavian and jugular veins. Death in two and one-fourth months. Autopsy.

No. 42.—Favier (Thèse de Lyon, 1903): Female, aged 66 years. Mitral insufficiency. Painful swelling in left neck. Collateral circulation. Skin red. Recrudescence after two and one-half months. Thrombosis of left jugular veins. Death in three months. No autopsy.

No. 43.—Desquiens (Bull. Soc. anat. de Par., 1904, lxxix, 429): Female, aged 22 years. Myocarditis. Painful œdema of right arm and neck. Palpable jugular cord. Collateral circulation. Thrombosis of right subclavian and jugular veins. Death in 19 days. Autopsy: Pulmonary infarcts.

No. 44.—Lacombe (J. d. Practiciens, 1904, 359): Female, aged 70 years. Mitral insufficiency. Painful swelling of right arm and neck. Palpable axillary cord. Thrombosis of right subclavian and jugular veins. Death in 32 hours. Autopsy.

No. 45.—Desquiens (Thèse de Par., 1906): Female, aged 43 years. Mitral insufficiency and adherent pericardium. Œdema of right arm and neck. Jugular cord. Fever. Thrombosis of right jugular and subclavian veins. Death. Autopsy.

No. 46.—Peters (Proc. N. Y. Pathol. Soc., 1909, ix, 149): Female, aged 38 years. History of several attacks of acute rheumatic fever during 20 years. Mitral insufficiency and stenosis. Painful swelling in left neck and axilla. Palpable jugular and axillary cords. Leucocytosis, 14,000. Fever. Thrombosis of superior vena cava, left innominate, jugular and subclavian veins. Death in three weeks. Autopsy.

No. 47.—Collet and Curtil (La Clinique, 1909, iv, 228): Female, aged 63 years. Fibrous myocarditis. Swelling of left arm, shoulder, breast and neck. Palpable jugular cord. Thrombosis of left subclavian and jugular veins. Death in six days. Autopsy.

No. 48.—Blumer (Yale M. J., 1908-09, xv, 296): Male, aged 12 years. History of acute rheumatic fever. Mitral insufficiency. Pain in left neck. Swelling of left neck and arm. Tender veins. Fever. Thrombosis of left subclavian and jugular veins. Death. No autopsy.

The following 17 cases have not been reported before, most of them occurring in the medical and pathological services of The Johns Hopkins Hospital.

No. 49.—(J. H. H. Medical No. 708): Male, black, aged 50 years. Aortic insufficiency, possibly of syphilitic origin. Thrombosis of right femoral vein. Death in one month. Autopsy: Pulmonary infarction.

Past History.—The patient had gonorrhœa and lues as a young man, and rheumatic pains from time to time in knees and elbows. The joints were never swollen.

Present Illness.—Onset was seven weeks before admission with shortness of breath on exertion, cough and expectoration. Three weeks before admission swelling of legs appeared, which increased during the last week. There was a diminished amount of urine. The abdomen was swollen and much distress was felt in the region of the heart.

Physical Examination.—On admission there was general anasarca, ascites, enlarged heart with signs of aortic insufficiency and gallop rhythm. The œdema diminished rapidly during the following week. One month after admission there was a recurrence of moderate œdema of the extremities and ascites. Two weeks later there was no very definite impulse on inspection or palpation of vessels of neck. Ten days later tenderness on motion of the calf and thigh muscles of the right leg developed. Œdema of the right leg appeared though there was none of the left. No difference was noted in the temperature of the two extremities. Sensation was normal. During the following month there was more or less persistent myocardial insufficiency. There was no fever. The patient died suddenly three months after admission.

Autopsy No. 149—Anatomical Diagnosis.—Acute and chronic endocarditis of the aortic valves; cardiac hypertrophy and dilatation, with relative mitral and tricuspid insufficiency; hydrothorax (right); chronic passive congestion of viscera; thrombi in right ventricle; femoral thrombosis (right); infarction of lung; gangrenous abscesses in lung.

Body.—The lower extremities, especially the right, are œdematous. There is a slight excess of fluid in the abdominal cavity, and 1400 cc. of fluid blood in the right pleural cavity. There are several firm, red infarcts in the left lung. In the branches of the pulmonary artery leading to these are firm, adherent, thrombotic masses. The surface of the right lung is covered by a fresh, fibrinous exudate, and there is a large area of infarction in the lower border. In removing the lung this was broken into, revealing a gangrenous cavity with ragged walls and foul contents.

The *heart* is very much enlarged and both sides are filled with clots and fluid blood. In the left ventricle near the aortic orifice there is a firmly adherent thrombus mass which is white and measures 5x3 cm. The aortic valves are much thickened. The heart muscle is firm, and of a dark red color. There are several small, fresh vegetations on the aortic valves. The other valves are normal. The length of the left ventricle is 9 cm., of the right 7½ cm. Thickness of the wall of the left ventricle is 18 mm. and of the right 6 mm. Weight, 530 gm.

The *femoral (right) vein* is occluded by a firm thrombus.

No. 50.—(J. H. H. Med. No. 1231): Male, black, aged 37 years. Myocardial degeneration. General anasarca. Fever. Thrombosis of right and left femoral veins. Condition not recognized clinically. Death. Autopsy.

Past History.—The patient had measles as a child. He has never been well since an attack of grip two years before admission. He has complained of cough and shortness of breath, especially during the previous six months, and of orthopnœa at night. He has had œdema of legs and ascites for the last three months, and fever.

Autopsy No. 196—Anatomical Diagnosis.—General pulmonary substantive emphysema; hypertrophy and dilatation of the right ventricle and auricle; fatty degeneration of left ventricle; chronic passive congestion of liver and spleen; ascites; anasarca; large ulceration of thigh and scrotum; thrombus of femoral veins.

Body.—There is marked œdema of both lower extremities. At the middle of the inner side of the left thigh is a very large, irregular, deep ulcer, 10 cm. in length and 9 cm. in breadth, extending down to the fascia covering the muscles. It is covered with a sloughing tissue and a red, œdematous granulation. There is a similar ulcer on the anterior surface of the scrotum, measuring 4 cm. in diameter. There is some œdema of the scrotum. The abdominal cavity contains 500 cc. of turbid, brownish-red, fluid. There are 100 cc. of yellow fluid in each pleural sac. The pericardium covering the right auricle is much thickened. The cavities of the right side of the heart are much distended and filled with a soft, cruor coagulum. The wall of the right ventricle measures 6-8 mm. in thickness, that of the left, 11-12 mm. The tissue has a pale, yellow-brown color, mottled with dark red dots and streaks. The heart weighs 360 gm. The coronaries are free of sclerosis.

The lungs are bound down by old adhesions. There is marked emphysema. On section the lung has a salmon color.

The other organs show chronic passive congestion.

There is no further note on the thrombus in the femoral vein.

No. 51.—(J. H. H. Med. No. 9282): Female, black, aged 17 years. History of two attacks of acute rheumatic fever six months before admission. Mitral insufficiency and adherent pericardium. Thrombosis of left innominate, subclavian, axillary and jugular veins. Fever. Death in two days. Autopsy.

Past History.—Measles, whooping-cough, chicken-pox, pneumonia one year before admission and a severe attack of inflammatory rheumatism. Nearly all joints were affected (swollen and tender). There was a second attack six months later with swollen, red, painful elbows and fever for one week.

Present Illness.—Onset, 11 months before admission, with shortness of breath on exertion and palpitation of the heart. Three months before admission pains over the heart, slight cough and expectoration. No swelling of the feet at that time.

Physical Examination.—On admission there was œdema of bases of lungs, enlarged heart, signs of mitral insufficiency and adherent pericardium. The heart's action was irregular. No œdema was present.

Later notes showed that the condition of the heart was considered serious.

Then ensued an attack of acute rheumatic fever involving both elbows and knees. There were definite signs of aortic insufficiency.

Seven weeks after admission and two days before death the left arm became œdematous, the face and legs puffy. On the day of death the feet and left arm were somewhat puffy as well as the face. The patient complained of severe headache. The exitus was very sudden. Moderate, irregular fever was present throughout stay in hospital.

Autopsy No. 1245—Anatomical Diagnosis.—Chronic aortic and mitral endocarditis; chronic adhesive pericarditis; cardiac hypertrophy and dilation; chronic passive congestion of the viscera; thrombosis of left innominate, internal and external jugular, subclavian and axillary veins.

No. 52.—(J. H. H. Med. No. 9423): Female, white, aged 35 years. History of eight attacks of acute rheumatic fever. Mitral and tricuspid stenosis and insufficiency and aortic stenosis. Thrombosis of left subclavian and jugular veins and both common iliac veins. Fever. Death. Autopsy.

Past History.—Diphtheria at 10; chorea at 11, associated with paralysis of right side and eight attacks of acute rheumatic fever.

Present Illness.—The patient was admitted two and one-half weeks after the onset with general nervous symptoms.

Physical Examination.—On admission there were profuse crackles throughout the lungs, an enlarged heart, a presystolic murmur terminating in an accentuated first sound. The pulse was rapid and irregular. No œdema was noted, except for the crackles in the lungs. The cardiac condition improved. Eight days after admission an attack of arthritis in the left ankle occurred. Eighteen days after admission uniform distension of the abdomen was noted. The liver dulness extended 5½ cm. below the costal margin in the right mammillary line. The liver was tender and showed intrinsic pulsation. The œdema of the lung increased. Twenty-two days after admission the patient complained of swelling of the left arm from the shoulder to the wrist, without tenderness. By the next day the swelling had involved the left side of the neck, pectoral and shoulder regions and extended down the left arm as far as the left elbow in front and nearly to the wrist on the dorsal surface. There was pitting on pressure, distention of the superficial veins and some tenderness. Twenty-seven days after admission the swelling in the arm had nearly disappeared, but the indurated swelling of the neck persisted. Thirty-six days after admission Dr. Osler made the following note: "Still a good deal of swelling over the shoulder and neck. Marked swelling along the jugular as high as the angle of the jaw. Fœtal heart rhythm at base of heart." Then followed a period during which the general condition improved very much. The œdema of the left arm came and went. Pain in the right half of the abdomen and tenderness over the course of the external iliac vein developed, as well as distension of the abdomen and œdema of the legs. At times there was more or less myocardial insufficiency. Eleven months after admission sudden pain and cyanosis developed in the left leg and foot. A diagnosis of embolism was made by Dr. Osler. No pulsation was made out in the left popliteal and posterior tibial arteries. Three and three-quarter years after admission a similar attack of pain in the right leg occurred. Following this no pulsation was obtained from either femoral or popliteal arteries, and great discoloration of both legs developed. Sudden death intervened three years and nine months after admission.

Autopsy No. 2458 (Dr. MacCallum)—Anatomical Diagnosis.—Chronic endocarditis; stenosis and insufficiency of the tricuspid and mitral valves; contraction of the aortic valves; hypertrophy of the heart; occlusion of the left jugular and subclavian veins with subsequent canalization; thrombosis of aorta and common iliac artery; infarctions of spleen and kidneys; chronic passive congestion of viscera; obesity.

Body.—There is a marked lividity of the legs—a bluish color extending over the thighs and even on the abdomen.

Thorax.—On dissecting out the superior vena cava, it is found that the branches that form the left jugular are much thickened and contracted.

On being followed up they are found to form a definite fibrous cord, which on section is seen to contain several small lumina full of fluid blood. The original lumen of the vein has entirely disappeared. On an attempt to open the vein the scissors pass into several small channels. Similarly in the subclavian vein there has been the same production of fibrous cords and canalization.

The *heart* is somewhat enlarged. The epicardial surfaces are everywhere smooth. The right side of the heart is especially enlarged. On opening the auricle it is found that the tricuspid orifice is narrowed to a diameter of 2 cm. and forms a slit-like orifice, 1 cm. in length. The chordæ tendineæ about this orifice are thickened and shortened. The pulmonary valves are normal. The endocardium on the right side is clear. The pulmonary veins are free from thrombi. The left auricular appendage contains a definite thrombus. The mitral orifice is narrowed by a thick contracted edge to a slit of about 2 x 4 mm. Here, too, the chordæ tendineæ are shortened and thickened. The aortic valves are extraordinarily scarred and contracted. The right auricular appendage is almost enveloped in the fat of the epicardium. The posterior coronary artery opens here at the sinus of Valsalva. The coronaries show no very marked sclerotic changes. The posterior and anterior coronary segments are especially contracted. The posterior coronary segment of the aortic valve is reduced in length to 4 mm. The edge is deeply eroded. All the valves are greatly thickened and bound together. In spite of all these alterations there is no great insufficiency apparent. The wall of the left ventricle measures about 12 mm. in thickness, that of the right ventricle about 5 mm. The right ventricle measures 8 cm. in length. The left ventricle measures about 6.5 cm. The muscle is cloudy and flecked with patches of gray opacity. There are no definite areas of fibrous myocarditis.

The *lungs* on section are moist, tough and rubbery, everywhere air-containing and deeply congested. The arteries are very sclerotic.

The *spleen* is enlarged and firm. On section several irregular red infarcts surrounded by a hemorrhagic zone are found.

The *liver* is slightly enlarged. The surface is mottled with yellowish and dark red markings. On section the lobules are distinctly marked out. They are yellowish in color, separated by a dark red tissue.

The *kidneys* are congested, and the left kidney shows several firm yellowish infarcts.

The inferior vena cava is clear throughout. The aorta, on the other hand, at the level of the inferior mesenteric artery is completely occluded by a thrombus. Below this at the level of Poupart's ligament on the left side the common iliac artery forms a large mass which is quite firm to the touch. Below Poupart's ligament the arteries again contract and are empty. On section of the inferior mesenteric artery it is found to be closed at its root.

The obliterated jugular vein shows microscopically the muscular wall of the vein, inside of which there is no thrombus but a firm connective tissue distending the original wall. The connective tissue is perforated with very numerous, irregular cavities lined with endothelium. There are also small, narrow vessels apparently both venous and arterial in character.

No. 53.—(J. H. H. Med. No. 9738): Female, black, aged 70 years. History of arthritis six months before admission. Myocardial degeneration. Thrombosis of femoral vein. Death. Autopsy: Thrombosis of right pulmonary artery.

Present Illness.—The patient had rheumatism six months previous to admission lasting one month, involving the right knee which was swollen and painful. She has been short of breath and has had occasional cough with expectoration. Seven weeks before admission, after exposure to cold, she noticed, in addition to intensification of the above symptoms, swelling of the abdomen, left leg and left arm. The swelling of the arm was less at night, that of the leg remained the same.

Physical Examination.—On admission there were scattered crackles throughout the lungs; the area of cardiac dulness was increased, and a soft, poorly transmitted, systolic murmur was heard. The pulse was rapid and irregular in force and rhythm. In addition there were ascites, œdema of the back of the abdominal wall, and of both legs, especially of the left. The course of the disease was afebrile.

The patient died four days after admission and seven and one-half weeks after the onset of the present illness.

Autopsy No. 1329—Anatomical Diagnosis.—Arteriosclerosis; chronic diffuse nephritis; cardiac hypertrophy; chronic passive congestion of the liver and intestines; thrombi in the right auricular appendage; thrombosis of the left femoral vein.

The *body* shows general œdema, especially of the subcutaneous tissues of the trunk. There are numerous varicose ulcers with scars over the left tibia. The peritoneal cavity contains two liters of clear fluid.

Heart.—The pericardium contains 200 cc. of clear straw-colored fluid. The epicardium shows numerous milky patches and occasional supra-arterial fibroid nodules of a rather diffuse nature. The heart weighs 470 gm. The heart muscle is firm and of a brownish color. The valves, aside from slight thickening, show no abnormality. The coronaries are slightly sclerosed. The right auricular appendage is firmly distended by an ante-mortem thrombus. There are many thrombosed arteries in the lungs, which arise from a large mass just at the bifurcation of the main pulmonary artery. There is no infarction. The liver, spleen and kidneys as well as the lung show chronic passive congestion.

The *right femoral vein* is patent. The *left femoral vein* is completely thrombosed, the thrombus distending the varicose dilatations that exist in the lower part of the vein. The thrombus extends up to just above Poupart's ligament. All the tissues of the legs are very œdematous. A small vein perforating the second left intercostal space near the sternal margin is much dilated and plugged with a thrombus mass.

Streptococcus pyogenes was isolated from the heart's blood, from the thrombi in the intercostal and femoral veins, as well as from the auricular appendage, pulmonary artery and femoral gland.

No. 54.—(J. H. H. Med. No. 10951): Male, white, aged 16 years. History of pneumonia at seven. Aortic and mitral insufficiency. Thrombosis of the left subclavian, axillary and brachial veins. Fever, leucocytosis and purpura. Death in 19 days. No autopsy.

Present Illness.—Two months before admission swelling of the feet, legs and abdomen developed, with constant shortness of breath, followed one week before admission by swelling of the face and hands.

Physical Examination.—On admission there was orthopnœa, Cheyne-Stokes respiration, cyanosis, and general anasarca involving the eyelids, face, arms, trunk and legs. In addition, the left hand and wrist were very markedly œdematous. There was œdema of the lungs, a wide area of cardiac dulness, a systolic murmur well transmitted through the axilla, a presystolic rumble, an aortic diastolic murmur and gallop rhythm. The day after admission the following note was made: "The left arm is very much more swollen than the right. The condition suggests venous thrombosis. The brachial vein is distinctly indurated and cord-like and rolls beneath the fingers." By the eighth day after admission the swelling of the left forearm and hand had increased and the axillary and brachial veins felt like firm, thickened rods. Fever, leucocytosis, jaundice, purpura, and pleural friction rub developed nine days after admission with pain and an increase in the swelling of the left hand, forearm and lower half of the upper arm.

On the day of death, 12 days after admission—19 days after the onset of the thrombosis, and two months and one week after the onset of present illness—the œdema of the left arm was sufficient to cause a splitting of the corium. The patient died in a condition of myocardial insufficiency. No autopsy was obtained.

No. 55.—(J. H. H. Med. No. 13023): Female, white, aged 57 years. History of arthritis seven years before admission. Mitral insufficiency. Fever. Death in six days. Autopsy: Condition not recognized clinically. Thrombosis of right and left femoral veins. Pulmonary infarcts.

Past History.—Patient has had measles, whooping cough, chicken-pox, typhoid fever, pneumonia, small-pox and scrofula. She was confined to bed for 10 weeks with rheumatism in the ankles and knees seven years before the present illness.

Present Illness.—The onset was five months before admission with swelling of the feet and legs, hacking cough with expectoration, shortness of breath on exertion and scanty micturition.

Physical Examination.—On admission there was cyanosis, dyspnœa, œdema of the lungs and fluid in the right pleural cavity. The cardiac dulness was not increased. The sounds were faint and a systolic murmur was present. There were marked arteriosclerosis, ascites and œdema of the lungs. Death occurred six days after admission with the patient in a state of myocardial insufficiency.

Autopsy No. 1752—Anatomical Diagnosis.—Chronic nephritis; arteriosclerosis; hypertrophy and dilatation of heart; general anasarca; thrombus of femoral veins; mural thrombi (right and left ventricle and auricular appendage); thrombotic occlusion of the branches of the pulmonary arteries; multiple pulmonary infarcts; hydrothorax with slight fibrinous exudate; atelectasis of lung; chronic passive congestion of viscera; healing infarcts in spleen and kidneys; mitral and tricuspid vegetative endocarditis.

Body.—The dependent portions are very œdematous. Œdema of the legs is especially marked. The peritoneal cavity contains a small quantity of somewhat bile-stained fluid. The right pleural cavity contains about two liters of a turbid fluid of a brownish color. The pleural layers are bound together by old adhesions, overlying which is a layer of fresh fibrin. The left pleural cavity is obliterated by old adhesions. Over the apex the pericardial layers are bound together by adhesions.

Heart.—The right auricular appendage is found filled with thrombus masses. The tricuspid valves are slightly thickened. Along the mitral valves corresponding to the line of closure there is a series of minute, ragged vegetations. The mitral valves are markedly shortened and thickened. The aortic valves are somewhat thickened but not deformed. Near the margin of the left coronary segment and the posterior segment are small verrucose vegetations. In the apical portion of the left ventricle is a small, globular thrombus projecting from the trabeculæ. A similar one is found in the right ventricle in the region of the conus. The heart muscle is rather mottled, grayish and opaque, and moderately soft. There are no definite areas of fibrous myocarditis. The coronary arteries are markedly sclerosed showing yellow patches on the intima. The heart weighs 520 gm.

Lungs.—The pulmonary artery contains a large thrombus mass which is well rounded towards the hilum. It extends into the branches of the pulmonary artery, to the wall of which it is adherent. These branches of the artery, however, are for the most part incompletely filled by the thrombus. The viscera show chronic passive congestion. There are one or two thrombi in the veins of the broad ligament. There is marked sclerosis of the femoral vessels. The femoral veins contain a fresh thrombus.

No. 56.—(J. H. H. Med. No. 15741): Male, white, aged 40 years. Myocarditis. Thrombosis of right jugular vein not recognized clinically. Death in two and one-half weeks. Autopsy: Pulmonary infarction.

Past History.—First admission: Patient had had measles as a child.

Present Illness.—The illness began six days before admission when the patient noticed that his feet, legs and thighs were swollen, and he had some shortness of breath. He has had a cough for the past six months with expectoration.

Physical Examination.—On admission there were cyanosis, œdema of lungs, enlarged heart, gallop rhythm, arterial hypertension, ascites and general œdema. Improvement was rapid with the disappearance of myocardial insufficiency. The attack was afebrile.

Second admission, No. 15973. Two months later a similar condition of myocardial insufficiency was present for about six days.

Physical Examination.—There was œdema of the lungs, enlarged heart, gallop rhythm, enlarged liver, but no ascites or œdema. The patient improved rapidly.

He began to work five weeks after the second discharge and continued for one year. For the last month he had shortness of breath, pain in the chest and swelling of the feet.

Physical Examination.—On the third admission there were œdema of the lungs, enlarged heart, gallop rhythm, arteriosclerosis, enlarged liver, ascites, œdema of legs. The patient did not improve. Two weeks after admission he had an attack in which he became very cyanotic, restless and had pain in the legs. The legs up to the knees and the hands were extremely blue. By the following day the œdema of the legs was markedly increased. There were jaundice, suppression of breath sounds and crackles at the bases of the lungs, with pleural friction in the right back, pulsating liver, and extreme myocardial insufficiency.

Death occurred two and one-half weeks after admission. There was a good deal of fever during the two weeks he was in the hospital.

Bacteriological examination at autopsy: Heart: *Streptococcus pyogenes.* Thrombus: *B. lactis ærogenes; B. proteus vulgaris, M. albus.* Peritoneal cavity sterile.

Autopsy No. 2458 (Dr. MacCallum)—Anatomical Diagnosis.—Arteriosclerosis of the coronary arteries; degeneration of the myocardium; hypertrophy and dilation of the heart; thrombus formation in the auricular appendage and left ventricle; chronic passive congestion of viscera; embolism of pulmonary and other arteries; hemorrhagic infarction of lungs; anæmic infarctions of spleen and kidneys; thrombosis of jugular vein (right).

Body.—The abdominal cavity contains a large amount of turbid fluid. The liver extends 15 cm. below the ensiform cartilage. The right pleural cavity contains about 800 cc. of fluid.

The heart is very much enlarged and weighs 530 gm. The right auricle is distended with a soft, post-mortem clot. The right ventricle is somewhat enlarged. Its wall measures 7 mm. in thickness. The tricuspid and pulmonary valves are delicate and competent. The right auricular appendage contains a post-mortem clot and also a softened ante-mortem clot. This is a typical thrombus composed of friable, grayish material with irregular superficial lines. On incision it shows a central cavity filled with a grayish-red, turbid material. The left auricle is normal in appearance. The left auricular appendage contains mostly post-mortem clots, but also another one of these softened thrombi. The left ventricle is dilated; its wall measures about 16 mm. in thickness. The mitral valves are normal throughout. At the apex of the ventricle is a mass about 22 mm. in diameter, which is rounded and projects from between the trabeculæ. This has a superficial network of projecting ridges which alternate in color from dark red to grayish-red. On section it is found to be softened in the center, so that the surface forms merely the capsule for a quantity of reddish-gray, thick, semi-fluid material underlying this thrombus. The heart muscle is rather opaque and yellowish. The aortic valves are delicate. The coronary arteries show sclerotic changes. The myocardium is rather soft and opaque. On tangential section it looks very cloudy and shows alteration of red or gray or even yellowish-gray patches.

Lungs.—On opening the arteries extending to the lower branch of the lower lobe of the right lung, numerous plugs of thrombus material with softened centers similar to those seen in the heart are found. These are continued by propagated thrombi into the smaller vessels. On the edges of the lower lobe are several areas which project somewhat and are dark red and covered with fibrinous exudate. These do not contain air and are of a deep red color on section. They are directly continuous with the occluded vessels; otherwise, the lungs are moist and contain air.

The *spleen* is enlarged, very firm in consistence. The connective tissue is increased. On section the pulp is dark red and cuts smoothly. The *liver* is large. On section it has a typical nutmeg appearance.

The *kidneys* are enlarged, very firm in consistence, and show numerous infarcts which vary considerably in size.

The right internal jugular vein is completely occluded by a thrombus.

No. 57.—(J. H. H. Med. No. 19287): Male, black, aged 46 years. Myocarditis, probably of syphilitic origin. Thrombosis of left subclavian and jugular veins. Discharged against advice.

Past History.—The patient has had six previous admissions with a diagnosis of arteriosclerosis and myocarditis. He had syphilis at 20.

Present Illness.—He was admitted with shortness of breath, swelling of the feet, legs, abdomen and left upper arm, which had developed gradually during the previous nine days.

Physical Examination.—On admission there were scattered crackles through the lungs; a wide area of cardiac dulness; a blowing systolic murmur, not well transmitted; a pulse irregular in force and rhythm, and general anasarca. The left supra-clavicular fossa was obliterated by a swelling which extended down to the left arm, and was most marked from the middle of the upper arm to the middle of the forearm. The superficial veins were markedly distended, especially the cephalic. The patient complained of pain and tenderness in the region of the left sterno-clavicular articulation, and in supra-clavicular fossa. Comparative measurements of the right and left arm were:

	R.	L.
Wrist	16 cm.	18 cm.
Elbow	27.5 "	33.5 "
Upper arm	27 "	34 "

After three days the swelling in the left arm still persisted, although the general anasarca had diminished. The heart's action remained irregular, and a blowing diastolic murmur had developed. The œdema of the lungs persisted. The following day the whole left shoulder and chest became fuller, the axillary folds were obliterated, the left external jugular stood out, the arm was much enlarged from the shoulder down. Just above the left clavicle, at the junction of its middle and inner thirds there was a firm mass, about the size of a pignut (2.5 x 2 cm.), suggesting strongly a thrombus.

The patient was discharged, against advice, 10 days after admission in the condition above described. He had had no fever.

No. 58.—(J. H. H. Med. No. 27065): Male, white, aged 49 years. Myocarditis. Thrombosis of the right innominate, jugular, subclavian, axillary and brachial veins. Fever and leucocytosis. Death in 48 hours. Autopsy. Pulmonary infarction.

Present Illness.—Onset was four months before admission with cough and dyspnœa. The latter was worse at night and accompanied by orthopnœa. On admission there were cyanosis and dyspnœa, scattered crackles through the lungs, rapid, irregular pulse, enlarged heart (no murmurs) and enlarged liver. The next day Dr. Barker noted marked dilatation of the left ventricle, gallop rhythm over the whole heart, enlarged and tender liver, œdema at the bases of both lungs and Cheyne-Stokes respiration. The patient's condition gradually became worse for the next three weeks. Then the temperature rose, leucocytosis developed and fluid collected at the right base. This was aspirated and had the character of a transfusion. Two days before death a swelling of the whole right arm was noticed. The next day it had increased and the firm, thrombosed, brachial vein could be traced into the axilla. The right external jugular stood out prominently as a thick cord. There was no tenderness in the course of these thrombosed vessels. Later small thrombosed veins were palpable over the right pectoral region and toward the thyroid gland. The thrombosis developed during extreme myocardial insufficiency and during an afebrile period. Blood cultures and cultures from the thrombosed veins *intra vitam* were sterile.

Autopsy No. 3524 (Dr. Winternitz)—Anatomical Diagnosis.—Chronic fibrous myocarditis; dilatation and hypertrophy of the heart; cardiac insufficiency; chronic passive congestion of viscera; multiple mural puri form thrombi of right and left ventricles; healed and healing anæmic infarcts of spleen and kidneys; thrombosis of right superior vena cava; propagated thrombus extending into the large veins of the neck and right arm; œdema of arm; multiple pulmonary emboli with multiple hemorrhagic infarcts of the lungs; acute pleuritis (right); hemorrhagic exudate; chronic splenic tumor; chronic perisplenitis; fatty degeneration of liver; chronic fibrous epididymitis; thrombi in the spermatic and prostatic veins.

The right portion of the thorax and right arm are very œdematous. Its circumference is half as large again as that of the left. The liver extends a hand's breadth below the costal margin in the mammillary line. On incision, a large amount of blood escapes. The right pleural cavity contains about 1 liter of blood-stained, brownish fluid in which definite flakes of fibrin are to be seen. In the upper portion of the anterior mediastinum the large veins stand out as dilated, firm masses. These dilated, firm cords involve the right innominate vein and all of its neck and arm branches. Along the course of the veins bulbous nodules protrude, which show definitely the valves within. The entire subcutaneous tissue in the region where these veins are thrombosed is very markedly œdematous, and on section one sees that this œdema is partly interstitial and partly due to a tremendous dilatation of the lymphatics, some of which in the region of the lymphatic duct and along the course of the subclavian vein and in the axilla are almost 1 cm. in diameter. They contain a clear, yellowish fluid. The pericardial sac contains only a slight amount of clear, straw-colored fluid. The parietal pericardium is normal in appearance. The visceral pericardium shows numerous, small ecchymoses over the right ventricle.

The *heart* is tremendously enlarged, and a few milky patches are found over the right ventricle. The right auricle is markedly dilated, and its wall thickened. The tricuspid ring is greatly dilated measuring 14.5 cm. in circumference. The valves are normal. The ventricle is likewise dilated. The columnæ carneæ are greatly hypertrophied and leave large pockets in which, especially at the apex, small, grayish, polypoid thrombi are found attached to the heart muscle. These contain, on incision, a small amount of reddish, softened material. The wall of the ventricle is otherwise smooth. The musculature is pale brown in color. The wall is thicker than normal, despite the great dilatation. The pulmonary valves are normal. No thrombus is found in the main branch of the pulmonary artery. The left auricle is not dilated; its wall is slightly thickened. The foramen ovale is closed. The mitral valves are large and show only slight sclerosis. The mitral ring is dilated. The left ventricle is greatly dilated; its wall varies much in thickness. Here again one finds large pockets between the columnæ carneæ, and in these are large masses of ante-mortem clot, which are of two general types; the one gray on the surface, the other softer and of a reddish color. On incision, many of them contain a turbid, reddish-brown fluid. The thickest part of the wall of the ventricle is the upper portion near the aortic orifice where it measures 15 mm., while down at the apex it measures only about 4 mm. The aortic valves are large and normally attached and show no marked abnormality. The base of the aorta likewise is not very abnormal. On incising the heart muscle at the apex one finds that it is studded with large, scar-like, translucent, gray masses which take the place of the muscle. The descending branch of the posterior coronary artery shows a few atheromatous scars on its surface, but these are not sufficient to interfere much with the size of the lumen. The other coronaries are similar.

Lungs.—In the anterior margin of the upper lobe there is a small, black, consolidated wedge-shaped area. The rest of this lobe contains air. In the lower lobe the surface becomes much more congested toward the base, and here one finds another consolidated area involving one-third of this lobe. On section through the lung, it is pale, grayish in color, except in the consolidated areas above described.

The right lung is very much more voluminous than the left. The upper lobe is bound down by a few adhesions; it is pale, and resembles the upper lobe of the left lung. The middle lobe is more voluminous than the upper and in the middle portion there is a large, black area standing out sharply from the surrounding, pale, grayish-pink lung tissue. The lower third of the lower lobe is entirely consolidated. Over the surface there is a granular, dry exudate which dulls the surface. On section through the right lung the middle lobe in the consolidated area is reddish-black, dry and stands up from the surface. Joining this definite area of infarction is an area of congestion, extending for some distance in the neighborhood. In this area thrombosed veins are visible, but no definite infarction has occurred. The lower half of the lobe is almost entirely involved by the infarct. Extending from the base of the lower lobe is a deep, reddish-black, dry mass with a rather sharp line of demarcation. Above this the lung tissue is firm, atelectatic and congested. On opening the vessels one finds that running to all of these consolidated areas in either lung are thrombi which are fresh and friable and entirely occlude the vessel. The lung tissue aside from these consolidated areas is dry, grayish-pink in color, with a definite increase in consistence and a rusty shimmer.

The *spleen* is enlarged and shows a small healing infarct, which appears as a depressed, yellowish zone, and on section is pyramidal in shape, surrounded by an area of congestion. At its base is a tiny occluded vessel. The spleen is deep purple in color, very firm, cuts with considerable resistance and shows an excess of fibrous tissue.

The *liver* collapses as soon as the great vessels are cut. It is deep reddish-purple in color. On section the lobules are distinct and are much smaller than normal. The zones about the hepatic veins are reddish-black and depressed, while around the portal veins they are yellowish and elevated. There is a considerable variation in the size of these two zones throughout the liver.

The *kidneys* show numerous infarcts and are markedly congested.

The veins around the prostate are thrombosed. The spermatic vein likewise contains a large thrombus mass which dilates the vein greatly, particularly at the region of the valves, where bulbous prominences are formed.

No. 59.—(J. H. H. Med. No. 27402): Male, white, aged 54 years. Myocardial degeneration. Thrombosis of left subclavian and jugular veins and of left femoral vein. Fever and leucocytosis. Recovery in one month. Pulmonary infarction.

Present Illness.—Patient was admitted to the surgical service with swelling of the left arm of 6 days' duration.

Physical Examination.—Firm, knotted cords were felt in the course of the axillary and brachial veins and their branches. The superficial veins over the shoulder were dilated. The external jugular vein was engorged and a prominent, firm cord was found at the base of the neck. Seventeen days later the left leg became swollen. There were fever, leucocytosis, cyanosis and dyspnœa. The heart's action was rapid and irregular. During the course of the illness the patient had an attack of pain in the left chest and expectoration of much bright red blood. Dulness on percussion and crackles at angle of left scapula were associated with this attack. The cardiac condition improved but the œdema of the leg was still present on discharge one month after admission.

No. 60.—(J. H. H. Med. No. ?): Female, white, aged 43 years. History of acute rheumatic fever at 20. Mitral insufficiency and stenosis. Thrombosis of right innominate, jugulars, subclavian, axillary and brachial veins. Fever and leucocytosis. Death in 22 days. Autopsy: Pulmonary infarction.

Past History.—There was a possible attack of acute rheumatic fever at 20.

Present Illness.—Onset was six weeks before admission with shortness of breath, orthopnœa, especially at night, swelling of ankles, cough and blood-stained expectoration.

Physical Examination.—On admission there were cyanosis, dyspnœa, an enlarged heart, irregular and rapid in action, a slightly enlarged liver, ascites, and œdema of the extremities. There were also signs of mitral insufficiency and stenosis. Six days after admission patient had three attacks, at 7.45 a. m., 9.15 a. m., and 9.55 a. m., of dyspnœa, cyanosis, cold sweating, irregular and weak pulse, dizziness, pain in the epigastrium and left axilla.

At this time measurements showed the right lower leg to be slightly larger than the left, and two very small, nodular areas were felt in the right external jugular vein. Twelve days after admission, the right arm and leg were more swollen than the left, pitting on pressure. The right external jugular vein was prominent and hard. The patient expectorated an abundance of frothy blood. The leucocytes were 24,000 and there was fever.

For a period of five days she was critically ill. The right chest, breast, arm and hand were œdematous and cyanotic. Thrombosis of the right external jugular vein was visible as a distinct thickening, palpable 5 cm. above the clavicle.

Sixteen days after admission there developed extensive œdema of the right cervical and pectoral regions, including the mammary gland, and of the entire right upper extremity, it being twice the size of the left. A definite thrombus was palpable in the right external jugular vein, extending 5 cm. above the clavicle. The superficial veins over the right pectoral region, right breast and upper half of the right upper arm were dilated and conspicuous. Blood cultures were negative.

Autopsy No. 3793 (Dr. Kline)—Anatomical Diagnosis.—Subacute endocarditis affecting the tricuspid, aortic and mitral valves, producing insufficiency and stenosis; pulmonary and splenic infarctions (organizing); moderate chronic passive congestion of viscera; central necrosis of liver; chronic atrophic endometritis and salpingitis; chronic adhesive peritonitis and pericarditis; moderate ascites; moderate pericardial and pleural effusion; diffuse tracheitis and bronchitis; œdema of lungs; thrombosis of transverse, scapular, external jugular and subclavian veins on right.

Body.—There is considerable general œdema. Fifteen centimeters above the olecranon the circumference of the right arm is 33 cm., and that of the left is 26 cm.; 15 cm. above the patella the circumference of the right leg is 53 cm., and that of the left is 49 cm. On opening the abdominal cavity a moderately increased amount of clear, yellow fluid is found. There is about 200 cc. of similar fluid in the left pleural sac. The pericardial sac contains about 80 cc. of clear, yellow fluid. There are localized fibrous adhesions covering an area of a few square centimeters over the left ventricle, binding the apex to the parietal pericardium.

The *heart* weighs 525 gm. The right auricle is considerably dilated and somewhat hypertrophied. In the tip of the auricle there is a fairly fresh, small thrombus. The tricuspid ring measures 10.5 cm. in circumference. The cusps are thin and delicate. At the junction of two of the cusps, however, there seems to be some shortening of the chordæ tendineæ, drawing the cusps to the ventricular wall, and the edge of each cusp is rolled up and thickened. The right ventricle is considerably dilated and hypertrophied. The papillary muscles are large. The left auricle is considerably dilated and somewhat hypertrophied. The mitral ring measures 8 cm. The valves and chordæ tendineæ are remarkably thickened and shortened. Along the line of closure of two of the cusps are several small, fresh, wart-like growths. The left ventricle is dilated and considerably hypertrophied. The papillary muscles are markedly enlarged and thickened. On section the cardiac muscle presents nothing strikingly abnormal. The aortic ring measures 7 cm. The cusps are thickened for about half of their extent and show along the line of closure of the three cusps a row of small, fresh, wart-like growths. The coronary arteries present no abnormalities.

Lungs.—Left lung. On section of the left upper lobe there is some congestion and marked œdema. Frothy fluid exudes on slight pressure leaving a residual rusty color. In the left lower lobe there is a large, consolidated patch, measuring 4 x 3.5 cm. This patch is sharply circumscribed and does not contain air. It is granular and of a purple color. In the right upper lobe there is a consolidated patch of similar character as that in the left lower lobe, the cut surface measuring 10 x 4.5 cm. This mass involves fully one-third of the lobe. In the lower lobe there is another patch 4 x 3.5 cm.

Spleen.—On the surface several yellow, opaque areas are visible. On section the organ is much firmer in consistence than normal. It presents a garnet-red color. There is a marked increase in the connective tissue and numerous, dry, yellow, wedge-shaped, opaque areas may be seen.

Liver.—On section the organ presents an irregular lobulation; the central veins are black and the parenchyma yellow. The amount of congestion varies in different portions of the gland.

The transverse scapular, external jugular and subclavian veins on the right are completely thrombosed, the subclavian and transverse scapular veins through their entire length and the external jugular for a distance of about 7 cm.

No. 61.—(J. H. H. Med. No. ?): Female, black, aged 23 years. History of acute rheumatic fever during the past two years. Mitral insufficiency. Thrombosis of both innominate veins, right jugular and subclavian, left external jugular veins and central vein of left retina. Fever and leucocytosis. Death in 28 days. Autopsy.

Past History.—The patient has had repeated attacks of tonsillitis, and arthritis during the past two years, involving both upper and lower extremities.

Physical Examination.—The patient was admitted in a state of myocardial insufficiency with orthopnœa, cyanosis, enlarged heart, tachycardia, œdema of the lungs, enlarged pulsating liver, ascites and œdema of the lower extremities. There were signs of organic mitral insufficiency and of relative aortic and tricuspid insufficiency. An irregular fever suggested a smoldering endocarditis, though repeated blood cultures were negative. The patient was never free from myocardial insufficiency. Twenty-eight days before death the right forearm and lower third of the upper arm became swollen. The superficial veins of the right shoulder and chest were dilated. There was œdema of both legs. Both external jugular veins were conspicuous, firm, and could be rolled under the fingers. The right face became swollen, especially the lower eyelid and cheek. There was a puffy swelling in the right supra-clavicular fossa, and whip-cords were palpable later in the right bicipital fossa.

The left optic disc 11 days before death was obscured in outline with an œdematous retina about it. Scattered red and white areas of hemorrhage and exudate could be seen. The veins, especially that leading from the upper temporal retina, were large, blue-black vessels without light streaks. Before death the right brachial and axillary veins, and the right jugular vein as far as the angle of the jaw became palpable.

Autopsy No. 3787 (*Dr. Davis*)—*Anatomical Diagnosis.*—Acute and chronic fibrous myocarditis; acute mitral vegetative endocarditis; thrombus formation involving the superior vena cava, innominate, axillaries and jugular veins; multiple emboli in spleen and kidneys with infarcts; arteriosclerosis; chronic passive congestion of viscera; healed foci at lung apices; chronic pleural adhesions; aneurysm of splenic artery; chronic fibrous perisplenitis; ascites; double hydrothorax; relative valvular insufficiency of heart; general œdema; bronchopneumonia.

Body.—There is marked pitting on pressure over the ankles. The face and upper thorax are cyanotic. The pupils are not equal. The left is dilated and much larger than the right. On opening the abdomen one finds a moderate amount of free fluid in the peritoneal cavity, which is clear and yellow. Both pleural cavities contain a large excess of straw colored fluid—about 500 cc. The left lung is much compressed.

The *heart* is enlarged, weighs 320 gm. The epicardium is smooth and glistening. The right auricle contains only a post-mortem clot. The tricuspid orifice admits five finger-tips and measures 13 cm. The tricuspid valve is delicate and appears normal. The pulmonary orifice measures 7 cm. The left auricle contains a few rather firm thrombi, but none of them are very adherent. The mitral ring also admits five finger-tips and measures 11.5 cm. The mitral valve is considerably shrunken and thickened along the edge. There are also to be seen a number of small, granular masses along the line of closure, which can be scraped off with some difficulty, leaving small ulcerated areas. There are also a number of similar vegetations attached to the chordæ tendineæ. The wall of the left ventricle is considerably hypertrophied and its cavity is larger than normal. The aortic ring measures 6 cm. The aortic valves are delicate and seem competent. The heart muscle on tangential section shows an extreme grade of fibrous change; the grayish looking fibrous tissue seems to occupy about one-half of the tissue. In some places it has a decidedly yellowish tinge. The coronary arteries are not occluded by emboli, but show a few fine yellow patches throughout their extent. The pulmonary arteries show no emboli after a careful search. The pulmonary veins appear normal and contain no thrombi.

The tail of the pancreas reaches to the hilum of the spleen, where it is adherent to a smooth, firm, round nodule measuring about 4 cm. in diameter. This nodule is closely attached to the spleen, and on section is seen to consist of a thin wall surrounding a cavity which is almost filled with laminated, blood-clot; the space which is not filled by blood-clot measures 1 cm. across. No connection is to be made out with what remains of the splenic artery. On incision of the lower branch of the splenic artery, it is found to be occluded outside of the spleen tissue for a distance of 2 cm. by a thrombus mass. This branch of the artery on being traced down from the thrombus to the spleen is seen to lead directly to the apex of the discolored area at the lower pole. On section that portion of the splenic tissue which lies under the discolored area at the pole is seen to be quite pale and yellowish looking, and has a distinct line of demarcation from the rest of the splenic tissue.

Left Kidney.—At the upper pole there is an area which is only slightly depressed, but which is of a bright yellow color, surrounded by an area of hyperæmia. This area, on section, shows beneath it a triangular yellow mass extending down to the medulla, and surrounded on all sides by an intensely hyperæmic zone. In this yellow area the striations and glomeruli are still to be faintly made out. On opening the superior vena cava there is seen a firm, rather light colored thrombus mass, extending almost to the opening of the right auricle. This thrombus mass, by palpation outside of the veins, is seen to extend into the innominate veins, the left external jugular and the axillary vein as far as it can be followed without cutting the skin over the arm. On the right it extends into the internal and external jugular veins and the axillary as far as it can be followed, and all the other small veins arising from this. (Permission was not obtained to open the neck.) The jugular bulb is removed for a distance of 2 cm. Beyond this point it can be felt as a firm cord extending up, as far as can be made out, into the upper triangle of the neck. The vena cava, innominates, axillaries and jugulars are removed *en masse.*

Microscopically the thrombosed veins show evidence of organization; but not of infection.

No. 62.—(J. H. H. Med. No. 29319): Female, white, aged 23 years. Mitral stenosis and insufficiency, possibly following puerperal infection. Thrombosis of left subclavian and jugular veins. Fever and leucocytosis. Death in 12 days. No autopsy.

Present Illness.—The cardiac condition became apparent during pregnancy. Two months before death, the patient was delivered of an 8-month child because of myocardial insufficiency. She showed cyanosis, dyspnœa, œdema of the lower half of the body, enlarged heart and gallop rhythm, signs of mitral stenosis and insufficiency, œdema of the lungs and ascites. Twelve days before death the left arm became œdematous, the hand puffy. The œdema extended under the clavicle to the supraclavicular fossa. There was some pain and tenderness in the arm, and the left breast became swollen. Leucocytosis and fever developed. In five days the thrombosed left jugular veins were palpable. The superficial veins over the left breast and shoulder were dilated. There was no evidence of embolism or infarction.

No. 63 (Blumer).—This is an unreported case occurring in the service of Dr. Daggett and we are indebted for the record to Dr. Geo. Blumer of Yale University who saw the patient.

Female, white, aged 50 years. Mitral insufficiency. Thrombosis of right subclavian and jugular veins. Fever. Recovery in two months.

Present Illness.—Patient noticed swelling of ankles 10 months before admission. Sudden dyspnœa, orthopnœa, cough, frothy expectoration, swelling of limbs, body and face, developed.

Physical Examination.—On admission there was an irergular, rapid pulse, enlarged heart, signs of mitral insufficiency and an enlarged tender liver. Later a right hydrothorax occurred. While the patient was in this condition soreness in the right neck and painful swelling of the right hand and arm developed. The right jugular vein was palpable as a tender cord. The œdema cleared slowly and was gone in two months. Fever was associated with the thrombosis.

No. 64 (Ellis).—For the records of this unpublished case we are indebted to Dr. A. W. Ellis, now of the Rockefeller Hospital, New York City.

Male, white, aged 46 years. Myocarditis. Thrombosis of right innominate, jugular and subclavian veins. Fever, jaundice and leucocytosis. Death in 10 days. Autopsy: Pulmonary infarction.

Present Illness.—Two months before admission the patient noted shortness of breath and palpitation, swelling of feet and occasional bloody expectoration. Two days before admission the right hand became swollen. On admission, the right hand and arm were œdematous as far as the shoulder. There was no pulse in the veins of the right neck. The right jugular vein was prominent, hard, and very tender. The heart was enlarged, but there were no murmurs, though the sounds were feeble and the action irregular. The arm continued to swell and became cold and cyanotic. The liver was enlarged and tender. Jaundice, leucocytosis and fever were noted. Blood cultures were negative.

Autopsy (Dr. Ellis)—Anatomical Diagnosis.—Chronic fibrous myocarditis; dilatation and hypertrophy of heart; chronic passive congestion of viscera; mural thrombus of right ventricle; extensive venous thrombosis beginning in the bulbus venosus and involving all of the distal veins; extensive embolism into the pulmonary arteries with massive infarction of the lungs; acute fibrinous pleurisy.

The *body* shows a general icterus. The lips are cyanotic. The right hand and arm are markedly œdematous and swollen, measuring about three times the diameter of the left, and pit on pressure. The right leg, foot and thigh are swollen and œdematous, pitting on pressure. There is a firm, hard swelling above the clavicle on the right side which is apparently the thrombosed bulbus venosus. The peritoneal cavity contains no excess of fluid. The liver extends 3 cm. below the costal margin in the nipple line. The left pleural cavity contains a few ounces of bloody fluid, and there are a few fine adhesions over both lungs.

The *heart* is enlarged and acutely dilated. It weighs 435 gm. All the cavities are markedly dilated and filled with post-mortem clot. The right ventricle contains a grayish-brown, friable, mural thrombus, covering almost its entire posterior surface for a thickness of about half an inch. The center of the clot shows puriform softening. The endocardium throughout shows marked bile staining. The tricuspid ring measures 13.5, the pulmonary 8, the mitral 12, the aortic 9 cm. in circumference, respectively. The mitral valve shows very slight thickening along the edge of its aortic segment. The aorta shows no arterial changes macroscopically, nor could anything be made out in the other great arterial trunks of the body.

Venous System.—The tibial, femoral and iliac veins show nothing abnormal. The inferior vena cava, portal, renal and superior cava are all free from thrombi. The right bulbus venosus, external and internal jugulars, axillary and brachial and radial veins are distended and filled with thrombus. The axillary and brachials show a marked irregular distension, firm nodules where the vein is half as large again occurring at fairly regular intervals throughout its length. These swellings occur at the situation of the valves. By far the larger portion of this thrombus is dark and soft, showing absolutely no sign of organization. It is only in the bulbus venosus that any sign of organization is seen. Here the clot is firm, pale in color, and firmly adherent to the vessel wall. The walls of the veins do not appear thickened.

Lungs.—The surface of the left lung is dulled, with occasional flakes of fibrin over it. A large portion of the lung, especially the lower part of the lower lobe, is consolidated. On section the whole lung shows a condition of massive infarction. The lower lobe is absolutely solid, dark red in color and does not contain air. The upper lobe shows large areas of complete hemorrhagic consolidation, but between them are small areas of lung tissue which contain some air. The pulmonary artery and its main branches show no sclerosis or thrombosis, only the small, terminal branches being filled with soft, dark thrombi. The middle lobe of the right lung shows a similar consolidation, while in the lower lobe a few small areas of air-containing tissue still remain. The upper lobe contains air. Here again the vessels are filled with thrombi.

No. 65.—(J. H. H. Outside case): No clinical notes.

Male, white, aged 70 years. Aortic insufficiency and adherent pericardium. Thromboses of right iliac and right brachial veins. Death. Pulmonary infarction.

Autopsy No. 3274 (Dr. Thomas)—Anatomical Diagnosis.—General arteriosclerosis; chronic diffuse nephritis; chronic aortic endocarditis with insufficiency; coronary sclerosis; chronic adhesive pericarditis; chronic passive congestion of viscera; ascites; hydrothorax; atelectasis and general anasarca; acute vegetative endocarditis (aortic and mitral valves); mural thrombi; pulmonary embolism; thrombus of the right iliac and right brachial veins; healing infarcts of lung; bronchopneumonia.

Body.—The skin over the body is very œdematous. The abdominal cavity contains an excess (500 cc.) of clear fluid. The right pleural cavity is filled with a clear amber colored fluid. The lung is compressed.

Heart.—The right auricle is dilated. The wall is thickened. The muscle bundles are quite plump. In the auricular appendage is a small, grayish-white body measuring about 4-8 mm., which is adherent to the wall and quite friable. The tricuspid ring measures 13 cm. The cusps are quite thin and delicate. There is no roughening seen at any place. The right ventricle is free from thrombi. The musculature is apparently normal. The pulmonary valves are delicate. The left auricle is dilated. The wall is thickened. The mitral ring measures 10 cm. On the aortic cusp is a small, grayish, translucent, nodular mass. The cusps of the valve are to a slight extent thickened. The left ventricle is free from thrombi. The aortic ring measures 8 cm. The valve leaflets are decidedly thickened. On the free margin of all three cusps are seen tiny, translucent bodies not more than 1 mm. in diameter. The heart muscle on tangential section is brownish-red in color. The muscle fibers are rather coarse.

Lungs.—In the right lung several thrombi in the pulmonary arteries lead to areas of hemorrhagic infarction.

The right iliac and brachial veins contain large thrombus masses which are grayish-yellow in color and friable.

ANALYSIS OF CASES.

Number of Cases.—There are 65 cases reported in the literature by 41 different authors. In many instances the details of the cases are meager, but in most the conditions are satisfied, which are necessary for including the cases in the series of venous thrombosis during myocardial insufficiency. Out of the possible 65 cases we have selected 48 which seem to fall in this group. The other 18 were excluded, because it could not be ascertained from the reports whether the thrombosis was associated with myocardial insufficiency or with some other condition such as tuberculosis, malignant disease, arteriosclerosis, aneurysm, or other more common cause.

The conditions which have been more or less arbitrarily chosen as requirements for including cases in this series are two: (1) That there was a definite myocardial insufficiency present at the time the thrombosis occurred; (2) That in all cases in which an autopsy was not performed, the diagnosis of the presence of a thrombosis was based upon unquestionable clinical observation.

In addition to these 48 cases in the literature there have been 17 cases observed in the clinics of the Johns Hopkins Hospital during the 24 years to date. Five of these cases were reported by Dr. Welch in 1900. One of the patients subsequently died and the pathological findings are here included. One other instance included by Dr. Welch has been excluded from this series, because the thrombosis was not associated with myocardial insufficiency. The series contains two other cases which we are allowed to report through the kindness of Dr. George Blumer, of Yale University, and of Dr. A. H. Ellis, now of the Rockefeller Hospital for Medical Research.

It is of interest to note that of the 17 cases from this clinic five were observed since our attention was drawn to the subject by one of the recent cases (No. 58) described above. Twelve of these cases have been observed, both clinically and pathologically; in one only the autopsy records were accessible.

ANALYSIS OF 65 CASES.

Age Decades	No. of Cases.
1-10	1
11-20	10
21-30	9
31-40	11
41-50	10
51-60	12
61-70	7
71-80	1
Not given	4

This table shows the unimportance of age in this relation. The earliest age is nine years; the oldest, 73 years. The condition may occur at both extremes of life. Between 10 and 70 the cases are equally divided as to decades.

Sex.—Forty-six of the patients were females, compared to 19 males. This is possibly partly explained by the frequency of association with mitral disease, a cardiac lesion notoriously more common in females than in males.

Etiology.—It is essential to attempt to determine the etiology of the underlying cardiopathy. How far it may have a bearing upon the cause of the associated venous thrombosis can only be conjectured but, as will be shown, the relation may be important. Of the 65 patients, 26 had developed valvular lesions during or after attacks of acute rheumatic fever, or at least gave histories permitting them to be classified as belonging to the rheumatic group. In two cases, the valvular lesions had followed an influenza; in one, a previous endocarditis; in two, puerperal infection; in one, scarlet fever; in two, syphilis, and in four, pneumonia. In many instances these infectious diseases dated several years before the thrombosis. In those with acute rheumatic fever, as this table shows, the limits were from six months to 40 years, with variation in the number of attacks.

Time Interval between Acute Rheumatic Fever and Thrombosis.	Number of Attacks of Acute Rheumatic Fever.
6 mos.	1 attack
9 "	?
10 "	2 attacks
1 yr.	?
1 "	2 attacks
1½ yrs.	2 "
2 "	2 "
2 "	1 attack
4 "	?
7 "	1 attack
7 "	?
7 "	3 attacks
9 "	?
16 "	?
17 "	?
20 "	?
23 "	1 attack
24 "	8 attacks
31 "	5 "
31 "	?
40 "	?
40 "	2 attacks

In four cases the time interval and numbers of attacks were not stated. In the other 12 instances of infectious diseases the time interval ranged from two to eight years.

While these intervals are long, still our knowledge concerning the chronicity of the infection associated with endocarditis and its tendency to recur in repeated acute exacerbations points to a persistence of the primary focus of infection and indicates that in many such diseases the infection does persist, however mild in virulence. In fact the milder the infection, the more likely it is to persist. This may be of great importance in determining the infectious agent responsible for the thrombosis. It seems noteworthy that so many of the cases were associated with some infection and in such a large number it was acute rheumatic fever.

Cardiac Lesion.—The cardiopathy underlying the state of myocardial insufficiency was as follows:

	Cases.
Mitral insufficiency	14
Mitral stenosis	6
Aortic insufficiency	4
Mitral insufficiency and stenosis	12
Aortic insufficiency and stenosis	2
Mitral and aortic insufficiency	3
Mitral and aortic stenosis	1
Mitral and tricuspid insufficiency and stenosis and aortic stenosis	1
Tricuspid stenosis and mitral and aortic insufficiency	1
Mitral insufficiency and aortic insufficiency and stenosis	1
Mitral insufficiency and stenosis, and aortic insufficiency and stenosis	3
Myocarditis	13
Not given	4

The mitral valve was affected in the largest number of cases.

	Cases.
Mitral valves alone	30
Mitral valves in combination	12
Aortic valves alone	6
Aortic valves in combination	10
Mitral stenosis alone and in combination	24
Mitral insufficiency alone and in combination	35

It is interesting to note that the preponderance of the cases are associated with valvular disease and relatively few with myocarditis. The valvular lesions occur in the relative frequency with which they are usually met, unaccompanied by any complications. This would lead one to believe that they do not have any important bearing upon the specific condition under discussion.

Localization of the Thrombi.—These may be briefly tabulated as follows.

Superior vena cava or both innominate veins and branches, 6 cases	
S. V. C.	3 cases.
R. and L. I.	3 "
Left arm and neck veins, 29 cases.	
L. I.	6 cases.
L. Subcl. and J.	14 "
L. Subcl.	8 "
L. J.	1 case.
Right arm and neck veins, 17 cases.	
R. I.	5 cases.
R. Subcl. and J.	8 "
R. Subcl.	2 "
R. J.	2 "
Combination of the two sides, 5 cases.	
L. Subcl. and J. and R. Subcl.	1 case.
L. Subcl. and R. Subcl.	1 "
L. Subcl. and L. F.	1 "
L. Subcl. and J. and L. F.	1 "
L. Subcl. and J. and L. and R. Fem.	1 "
Iliac or femoral veins, 7 cases.	
Both sides	4 cases.
Left side	2 "
Right side	1 case.
Not given	3 cases.

The most interesting facts derived from the above analysis are the relative number of cases in which the thrombosis involved the veins of the upper extremities as opposed to those of the lower. Of the 65 cases, in only seven did it occur in the lower extremities alone. In three other cases the veins of both upper and lower extremities were thrombosed. Secondly, of the 57 cases in which the veins of the upper extremity were involved, both were affected in eight cases. In the remaining 49, the right side was affected in 17, and the left in 32 cases.

While these figures give a predominance to the localization of the thrombosis in the veins of the left upper half of the body, still it is believed this is due to insufficient statistics. In our own cases the right upper extremity was involved to a greater extent than the left. This is of importance, since the process has frequently been attributed to a mechanical condition present only on the left side. For the above figures such an explanation is, of course, quite inadequate.

Clinical Evidence of Infection at the Time of Thrombosis.—Data concerning infection at the time of the thrombosis were lacking in most of the case reports.

	Cases.
Fever alone	12
Fever and leucocytosis	5
Fever and jaundice	1
Fever, jaundice and sweats	1
Fever, leucocytosis and purpura	1
Chills	1
Fever, leucocytosis and pleurisy	4
Acute fibrinous pericarditis and pleurisy	1

Even though these cases have no absolute value as evidence of the infectious nature of the thrombosis, still they form the only clinical evidence of infection present at the time of the thrombosis, which may be gathered from the reported cases. Infection seems to be of so much importance in our knowledge of thrombosis in general, that these data are worthy of emphasis here.

In only two cases were organisms recovered by culture: in one, streptococci from the heart's blood; in the other, streptococci from the thrombus. Such really positive evidence is difficult to obtain. In four of the recent five cases blood cultures *intra vitam* and cultures at autopsy proved sterile. In one, cultures made before death from a puncture of the thrombosed veins gave no growth.

Clinical Symptoms and Signs of Thrombosis.—Œdema is by far the most common and not infrequently the only manifestation of the venous thrombosis. Local pain and tenderness over the veins and palpable whip-cords in the course of the vessels were the next most frequent indication of the condition. Cyanosis and local coolness to the palpating hand, evidences of collateral circulation, loss of the jugular pulse, unilateral exophthalmos and torticollis were among the other symptoms noted.

Three cases were not recognized clinically. In two of these the veins of the lower extremity were involved, in the other the jugular. General anasarca was marked in all three. It is our impression that it is quite impossible to recognize this condition when the veins of the legs are involved and the general œdema marked. An aid to diagnosis was emphasized in one case. The anasarca disappeared during the night and returned during the day in the entire body, except in the left leg where the swelling remained constantly the same.

An interesting fact from the above analysis is that the œdema may frequently be the only sign of the condition. This supports the idea that the condition may readily be overlooked and the distribution of the œdema considered only a mechanical effect of gravity resulting from the insufficiency of the heart muscle. Careful observation of such cases, however, will show that the œdema resulting from the thrombosis is a persistent phenomenon, and usually a residue, when the œdema elsewhere in the body, the pure effect of the myocardial insufficiency, is disappearing.

Result.—As far as the records reveal, the mortality in the 65 cases was 83 per cent (54 cases). One patient was discharged against advice and lost track of. The remaining 9 patients were considered recovered. However, in six of these cases the period of observation was only from three weeks to three and a half months. In the other four no statement is made aside from the fact that they "recovered."

The condition then is an extremely fatal one. In 44 cases the interval between the onset of the thrombosis and death is known.

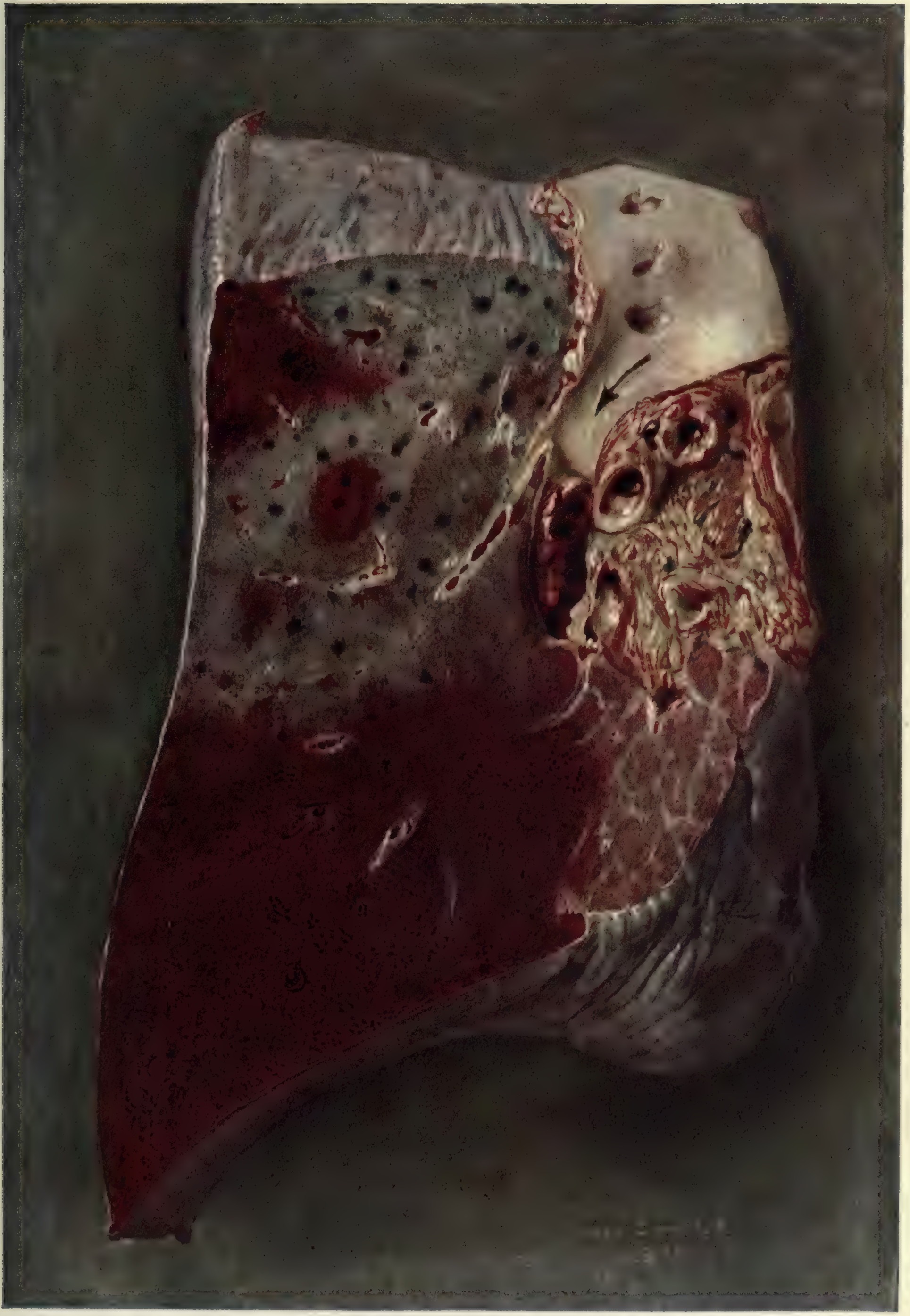
In	1 case	death	followed	in	1 day
"	6 cases	"	"	"	2 days
"	1 case	"	"	"	3 "
"	1 "	"	"	"	4 "
"	3 cases	"	"	"	6 "
"	3 "	"	"	"	1 week
"	1 case	"	"	"	10 days
"	5 cases	"	"	"	2 weeks
"	15 "	"	"	"	3 to 4 weeks
"	1 case	"	"	"	6 weeks
"	5 cases	"	"	"	2 to 5 months
"	1 case	"	"	"	6 months
"	1 "	"	"	"	3¾ years

Except for this last case, which remained under constant observation for three and one-half years, the interval was fairly short. Thirty-six of the 45 patients died within a month after the onset of the thrombosis.

Pulmonary embolism and infarction are the most serious complications, making the complication a particularly serious one. Pulmonary infarction occurred in 27 cases and every one of these was fatal. It is striking that no patient that recovered gave evidence of pulmonary infarction at any time. If infarction does not occur, then the determining factor in the outcome is the underlying cardiac condition or the associated infection.

REFERENCES.

BOUCHUT: Gaz. méd. de Paris, 1845, xiii, 2^me^ s., 245.
PETER: Leçons de clinique méd., 1873, i, 209.
HANOT: Compt. rend. Soc. de biol., 1874, i, 6^me^ s., 80.
PARMENTIER: Arch. gén. de méd., 1889, ii, 91.
HIRSCHLAFF: Inaugural Diss., Berlin, 1893.
BALDWIN: J. Am. M. Ass. 1897, xxix, 371.
POYNTON: Lancet, 1898, ii, 206.
GALLAVARDIN: Province méd., 1899, xiii, 409.
——— Lyon méd., 1900, xcv, 10.
WELCH: Trans. Ass. Am. Phys., 1900, xv, 448.
——— Jacobi's Festschrift, 1900, p. 463.
HUCHARD: Traité des maladies du coeur 3^me^ éd., 1905, iii, 581.
BLUMER: Yale M. J., 1908-09, xv, 296.



Chronic Passive Congestion. Embolus and Hæmorrhagic Infarct of the Lung.

LEUKÆMIA OF THE FOWL: SPONTANEOUS AND EXPERIMENTAL.* †

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I. Review of the Literature.

The first publication was made by Moore[1] in 1895-1896, in which he reported observations upon an epizootic disease of fowls which he designated "infectious leukæmia." His studies were based upon cases obtained from five different outbreaks, and upon those artificially produced by means of the specific organism (Bacterium sanguinarium) isolated from the organs of these fowls. The descriptions of the spontaneous and experimental cases clearly show that he was not dealing with a true leukæmia of the fowl, but rather with an acute infectious disease, characterized by fever, diminution in the number of red blood cells, and increase in number of white blood cells, this increase being "restricted" to the polymorphonuclear leucocyte with the eosin staining spindles, *i. e.,* the phagocyte of the normal fowl's blood.

Butterfield,[2] in 1905, reported three cases of aleukæmic lymphadenoid tumors of the hen. His studies were limited to the livers of these animals. They correspond in every detail, both grossly and microscopically; were uniformly and strikingly enlarged (340, 420, 270 gm. respectively) and of a diffuse, light, cream, yellow color. Histologically, the liver tissue was extensively replaced by large oval or round, sometimes irregular, collections of cells. The intralobular capillaries were filled with the usual nucleated red blood cells. Most of the nodules of tumor cells were thought to be in connection with the portal spaces. The cells resembled in general the "large

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lymphocyte" of the hen's blood.* Allowing for flattening due to pressure, these cells were round or oval, with round or oval nuclei, mostly eccentric. The nuclear chromatin appeared granular or reticular. The nucleus was not infrequently pale and vesicular with one or more bright chromatin bodies. The cytoplasm was present as a narrow rim, non-granular, and basophilic. Mitoses were common. Between these cells was seen a delicate reticulum. In association with these tumor masses were quite large collections of eosinophilic cells, the majority showing a single, pale, round or oval, eccentric nucleus and a relatively abundant cytoplasm, filled with large, round, elongated, or spindle-shaped oxyphilic structures. They varied greatly in size and shape. The lymphocytes and eosinophiles were occasionally seen in the capillaries, but there was "certainly no definite increase within the blood-vessels." From the character of the cells, their relation to the portal spaces and absence of the lymphæmia, the condition was regarded by Butterfield as a proliferation of periportal lymphadenoid tissue, and thought by him to merit the designation "aleukæmic lymphadenoma."

Mohler had under observation five similar cases showing lymphæmia and the same lymphadenoid condition. Mohler's description of two of his cases, as presented by Butterfield, is as follows: The process showed a tendency to involve several organs. In one case the liver and spleen were the principal seats, the lungs and intestine were also involved. The liver was enlarged to twice the normal size, of very light color and mottled. Throughout its surface and within its parenchyma were whitish lymphomatous deposits of varying diameters. A section shows the liver tissue only partly obliterated as a result of a filling up of the interacinous capillaries with leucocytes. The spleen was about the size of an ordinary blue plum. Each lung contained a white spherical area, the size of a pea and composed of hyperplastic lymphoid tissue, infiltrating white cells. In the wall of the large intestine, involving the lymphadenoid tissue, were round, slightly raised nodules. In the second case the changes were most marked in the kidney and spleen. The liver, intestine and heart were also involved. The kidneys were three or four times the normal size and had macroscopically very much the same appearance as the liver in the first case. The myocardium contained some small, whitish areas. Butterfield, in comparing the histological findings in Mohler's cases with his own, finds a convincing similarity between, or identity of, the infiltrating cells. In Mohler's cases, the infiltration was more diffuse and not so regularly arranged about the portal tissue. Above all, the white blood cells were markedly increased in all the blood-vessels, from the intraacinar capillaries to the largest veins. The predominating white cell was indistinguishable from the cells in the tumor masses of both these and Butterfield's cases. From the foregoing, Butterfield felt justified in granting "the existence of a leukæmic and aleukæmic lymphadenoid hyperplasia in hens."

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* **Obviously the large mononuclear cell of the classification presented in this paper.**

Butterfield and Mohler deserve the credit of showing that leukæmia occurs in the fowl. Their studies were limited to post-mortem findings.

To Warthin,[8] in 1907, we are indebted for the first complete study of this disease in fowls. He had the good fortune to secure a living animal, which he kept under observation for two and a half months before it died. During this time he had an opportunity of carefully studying the clinical course. The blood showed a great reduction in the total number of red blood cells. These varied greatly in size and shape, and contained less hæmoglobin than normal. The total number of white cells was greatly increased. Differential counts showed a striking increase of the "large lymphocyte" at the expense of the other cells of the normal blood. Numerous mononuclear forms of the eosinophiles, cells abnormal to the blood, were seen. From the blood changes Warthin felt justified in making a diagnosis of "lymphatic leukæmia of the large cell type." A careful autopsy revealed the following findings: The liver was greatly increased in size and was pale yellow in color. The spleen and kidneys were also enlarged; both showed numerous yellowish spots from pin-point to pin-head in size. In the hæmolymph nodes small yellowish nodules were found. The bone-marrow appeared as solid plugs, reddish-yellow and friable. The tissue changes were summarized as follows: (1) Tumor-like nodules and infiltrations of lymphoid cells in all the organs, particularly in the liver, spleen, kidneys, bone-marrow and hæmolymph nodes; (2) replacement of the normal white cells of the blood by cells of the large lymphocyte type, more or less atypical in character, but identical with cells in the tumor masses. From the findings, both in the blood and in the tissue, Warthin made the diagnosis of leukæmic lymphocytoma.

He likewise examined the material from two additional cases of lymphadenoid tumors of the fowl. One proved to be of the aleukæmic type, as described by Butterfield; the other was of the leukæmic form, as described above. The histological picture, apart from the increase of white cells in the blood-vessels in the one case, was identical in both cases and also with that in the cases given above (Butterfield's, Mohler's and Warthin's). From these cases Warthin concludes, therefore, that there occurs in the common fowl a condition of disseminated lymphocytoma, sometimes aleukæmic, at other times associated with an increase of the white cells of the blood, this increase consisting in the appearance of great numbers of cells of the large lymphocyte type and apparently identical with the lymphoid cells of the tumor nodules. He also regards the aleukæmic and leukæmic conditions as genetically related, if not actually one and the same process in different stages. Both conditions, he thinks, are in all respects analogous to the similar ones existing in man.

The preceding cases appear to be very similar to those reported by later investigators and designated by them as splenomedullary in type.

Kon[4] in 1907, after the appearance of Warthin's article, reported what he considers a true case of leukæmic disease of the chicken. The gross and microscopical changes, which were studied and reported in great detail, are in general identical with those of the cases above. In addition, he found giant cells, though only a few, in the bone-marrow, and mitoses in the basophiles as well as in the eosinophiles in the kidneys. Because of the lack of smears, he determined the ratio W/R and made differential counts from sectioned blood-vessels of the liver. He found that the white cells, as compared with the reds, were greatly increased and that the large mononuclear was the predominating cell of the whites. Mitoses of this cell were observed. The evidence given, he thinks, is sufficient to consider this a case of true leukæmia. Because of the enormous swelling of the spleen and the plentiful occurrence of the characteristic cell in the pulp of the normal spleen and to a lesser degree in the normal bone-marrow, and in the absence of lymphatic swelling and the occurrence of this cell in the normal lymph tissue, it seems to him most likely that this is a case of true "splenic leukæmia."

Soshestrenski,[5] in May, 1908, reported a case of spontaneous leukæmia of the fowl, very similar to the case described by Kon.

His study was limited to gross and microscopical findings at autopsy. The bone-marrow was omitted. The contents of the blood-vessels of the organs were found to be leukæmic. He designates the case also as "splenic leukæmia," but in so doing he calls attention to the fact that the process involves many of the other organs and appears to be only primary and most marked in the spleen. There was no enlargement of the lymph-glands.

With Ellermann and Bang,[6, 7] in 1908, the subject takes on a different phase. Up to this time, the communications dealt entirely with the recording of spontaneous cases of leukæmia in the fowl. Ellermann and Bang were the first to successfully transmit the disease by experimental inoculations from a spontaneous case to other, healthy, fowls. In fact, they claim to have been the first to successfully produce the disease experimentally in any animal. They report the findings in two typical spontaneous cases giving identical pictures. The blood study during life was found to be practically the same as that of Warthin's case, with the exception that the large mononuclears frequently contained in their cytoplasm many granules, and thus represented cells which are not found in the normal blood—myelocytes. Small granules alternated with very large ones. The autopsy showed an enlarged spleen and liver, the latter with white dots and streaks. The bone-marrow was gray-red. The other organs presented nothing of interest. The microscopical changes were very similar to those of Warthin's case. The experimental leukæmia they transmitted to the third generation, producing a blood picture and organic findings identical with those of the spontaneous cases.

Pseudoleukæmia, which is characterized by the same organic lesions as are found in true leukæmia, but in which the blood picture is normal, they found to occur spontaneously among chickens. They received from the same flock, at the same time, a leukæmic and pseudoleukæmic animal. From the pseudoleukæmic animal, by inoculation, they produced a leukæmic animal, and conclude, therefore, that the leukæmia and pseudoleukæmia of chickens are etiologically identical.

Multiple sarcomatosis of the peritoneum occurs epidemically in the fowl. They consider this a manifestation of leukæmia, because by inoculation from such a case they produced an atypical leukæmia and carried this to the second generation.

They were successful in two out of five inoculations with a filtrate from an emulsion passed through a "Kerze aus Infusorierde" and conclude, therefore, that a cell-free filtrate is effective and that the cause must be an organized virus.

In the same year, Ellermann and Bang[9] reported that the blood of leukæmic fowls contained the virus. They also showed that among transmitted cases the disease may appear as a typical leukæmia or as a pseudoleukæmia, or only as an anæmia with changes in the bone-marrow. The injection of five animals with a Berkefeld filtrate resulted in one early leukæmia. The injected fowls were isolated and great care was exercised during the experiment.

The following year, 1909, Ellermann and Bang,[10] reported the transmission of the disease into the sixth generation, and also an additional positive Berkefeld filtrate series. Because the disease can be produced by a cell-free filtrate, they conclude: (a) Leukemia must be an infectious disease; (b) it is to be placed among the diseases due to a filterable virus. They call attention to the fact that mitoses in the blood are pathological and always present in leukæmia.

Schriddle,[11] in 1909, was the first to question whether, in leukæmia, we are really dealing with an infectious etiology. Basing his conclusions upon experimental work, he claims that chickens, injected with extracts of entirely normal organs, present the same changes as Ellermann and Bang have reported for leukæmia. He thinks that their findings are not leukæmic and that, therefore, there is no proof in favor of the infectious etiology of this disease.

Hirschfeld and Jacoby[12] in 1909, report a spontaneous case of leukæmia showing changes in the blood and organs which, they claim, agree entirely with the description of Ellermann and Bang. In a second case, the blood picture, although not typical, appeared to them leukæmic. At autopsy this fowl showed a typical chicken tuberculosis. They succeeded in transmitting this tuberculosis, in association with the apparently leukæmic blood picture, into the fourth generation. They did not know whether they were dealing with a combination of tuberculosis and leukæmia in the same animal, or with pure tuberculosis. An animal injected with a pure culture of the chicken tubercle bacillus developed a blood picture identical with that of the second spontaneous case. Therefore it seems highly probable that this case may have been one of pure tuberculosis. At any rate, it cannot be accepted as a definite and pure case of leukæmia.

The following year (1910) the same authors[14] report the injection of fowls subcutaneously from their first spontaneous case. They obtained no takes and their strain died out. From a leukæmic animal given to them by Ellermann and Bang, they transmitted the disease into the fifth generation, obtaining both leukæmic and pseudoleukæmic cases. In the blood, they found normoblasts and megaloblasts, *i. e.* small and large, round, nucleated, mostly polychromatophilic red blood cells. Although they state that the disease begins in the bone-marrow, they leave it an open question whether in the chicken one is dealing with a myeloid or a lymphoid leukæmia.

Burckhardt,[15] in 1910, advanced the theory, based upon investigations of his own on transmissible chicken leukæmia, that a particular leukæmic virus does not exist, and that in the so-called chicken leukæmia one is very probably dealing with a very chronic chicken tuberculosis. As proof, he claims that with a pure culture from such an animal (leukæmic) and also with older pure cultures of chicken tubercle bacilli, one can produce the same blood picture described by Ellermann and Bang for chicken leukæmia. The anatomical findings, he states, likewise correspond. Gratz[15] suggested that possibly in the culture of chicken tubercle bacilli from the leukæmic animal, there may have been cultivated, in addition to the tubercle virus, also the virus of leukæmia. Friedberger[15] considered this objection invalid, because, as he claimed, one could produce the leukæmic blood picture also by using old laboratory tubercle cultures.

Burckhardt,[16] in 1912, still adheres to his theory, but admits that he is unable ever to bring the blood into a leukæmic condition by inoculating with tubercle bacilli.

Hirschfeld and Jacoby[17] in the same year inform us that they presented to Burckhardt and Friedberger the chicken with which these investigators started their transmissions, and that on the day of delivery it showed a pronounced leukæmic blood picture. The animal, in addition, surely had tuberculosis, because all the transmitted leukæmic animals of the stock from which this animal originated had tuberculosis. They feel confident that in Burckhardt and Friedberger's stock the tuberculosis had crowded out the leukæmia, until finally only tuberculous and not leukæmic animals were obtained. They had a similar experience with the stock from which Burckhardt and Friedberger's animal originated.

Against the existence of an etiological relationship between tuberculosis and leukæmia, they present the following arguments: (1) The blood picture in tuberculosis is never to be confused with that of leukæmia. It is characterized by a hyperleucocytosis due to the polymorphs. (Ellermann and Bang [10] had also stated this fact at an earlier date.) (2) The organs of the tuberculous chickens were entirely free from the changes which Ellermann and Bang, and they themselves, found to be characteristic of leukæmia and which correspond entirely with leukæmic lesions in man. (3) By injections of organic emulsions obtained from spontaneous tuberculous chickens, or of pure cultures of chicken tubercle bacilli, they uniformly produced a typical tuberculous blood picture and organic changes, always without any signs of leukæmia.

Ellermann [18] [19] in 1913 and 1914, in answer to the question whether this chicken disease is really leukæmia, shows that it has all the symptoms of human leukæmia. He meets Schridde's objection by the argument that this investigator's claim was limited to the blood picture, and in the absence of the characteristic organic changes, of which he makes no mention, his experiments are of no importance. The injection of an organic emulsion Ellermann never found to cause any change in the blood, provided the material was not virulent. Ellermann and Bang had previously produced the disease with Berkefeld filtrates in three different experiments. In this paper Ellermann reports two more successful series. All other investigators have had only negative results. Thus, Hirschfeld and Jacoby [17] were unsuccessful in two experiments and Burckhardt [16] in one.

Ellermann is convinced that the filtrate experiments prove the theory of infection, for all the cells were surely removed. He feels that the fact that the virus passed through a rather thick-walled Berkefeld filter demonstrates that it is an invisible filtrate virus. He clearly shows that the leukæmic virus can be separated from the virus of tuberculosis by filtration and that, therefore, the two diseases are distinct. Starting with an emulsion of spleen taken from an animal, both leukæmic and tuberculous, in which tubercle bacilli had been demonstrated, he passed this through a porcelain (Reichel) filter and with the filtrate he produced leukæmia with complete absence of tuberculosis in all the inoculated animals.

Ellermann finally states that both the spontaneous and the transmitted leukæmia occur in two types; (a) myeloid, (b) lymphatic. In the first the blood is characterized by the presence of numerous myelocytes and transitional cells, occurring in association with a pronounced myelosis (large deposits of myelocytes) in the organs. In the second, the blood is characterized by a predominance of small and large lymphocytes (90 per cent of the total number) occurring in association with a pronounced lymphomatosis (numerous infiltrations with lymphoid cells) of the organs. Of interest is the fact that a myeloid type may occur in one generation and a lymphatic in the next, or that both types may occur in the same generation. The occurrence of both types in the same stock suggests very strongly that both forms of leukæmia in man are due to one and the same infection.

II. Studies on the Normal Fowl.

With the hope of making the findings in the leukæmic animals more clear, the following brief data of the normal fowl are presented. These are limited to those portions of the body which are involved in leukæmia. They are compiled from a large number of chickens.

EXTERNAL APPEARANCE.

Healthy, young, adult Plymouth Rock hen. Comb, featherless area about eyes, and wattles bright red. Conjunctivæ and buccal mucous membrane pink. Skin of body white with a faint yellow tint. Well nourished, sides of sternum covered with a thick pad of tissue, ribs not palpable. Average rectal temperature, 42 ° C.

BLOOD.

The blood for counting and smears was obtained from the vein under the wing, which always appears to be well filled. From a small needle puncture the blood flows under pressure, is thick, dark red and clots quickly.

Blood-count.—The nuclei-containing red blood cells of the fowl make it practically impossible to count the white blood cells by the usual direct method. After laking the former, one cannot differentiate between the nuclei of the two types of cells. It was therefore necessary to resort to the indirect method, *i. e.*, to determine the proportion of white to red cells from a stained smear, count the total number of cells, both whites and reds, by the direct method, and then calculate the total number of each present.

The red blood cells vary somewhat: lowest limit, 2,500,000; highest, 4,500,000; average, 3,000,000-4,000,000 per c. mm. White blood cells:

the extreme limits are between 20,000 and 80,000 per c. mm. Proportion of whites to reds, lowest limit, 1/40; average, 1/50-1/150.

Hæmoglobin (*Sahli*).—This shows considerable variation, lowest limit, 45 per cent; highest, 75 per cent; average, 60-70 per cent.

Blood Smears.—Wilson's stain was found to give the best results, especially when applied immediately after the smears were made.

Classification of blood cells (Fig. 1).

Erythrocyte.

1. Normocyte (*a*): Elliptical disk. Nucleus, same shape as cell, deep blue, slightly picnotic. Cytoplasm yellow and glassy. (Both cell and nucleus uniform in size, shape and staining).

Blood Platelet (*b*).

Length of normocyte, width less than that of normocyte. Nucleus round, purple, chromatin diffuse, diameter equal to width of its cell. Cytoplasm pale gray with vacuoles about nucleus, frequently containing small circumscribed red structures. May vary in size and shape.

Leucocytes.

1. Polymorphonuclear leucocyte with eosinophilic rods (*c*): Round, diameter about length of normocyte. Nucleus has two or more lobes, pale blue, chromatin diffuse. Cytoplasm colorless with bright red, spindle-shaped rods.

2. Polymorphonuclear leucocyte with eosinophilic granules (*d*): About the same in shape and size. Nucleus has two or more lobes, purple, slightly picnotic. Cytoplasm faintly blue with dull red granules.

3. Lymphocyte (*e, e′*): Round, diameter about width of normocyte. Nucleus round, purple, chromatin diffuse. Cytoplasm small in amount, to one side of nucleus, pale blue. Same cell may be slightly larger. Thus a division into the small (*e*) and large (*e′*) lymphocyte may be made.

4. Large mononuclear cell (*f*): Round or oval, diameter about length of normocyte (at times, more or less). Nucleus round, oval or slightly irregular, and larger, otherwise similar to nucleus of lymphocyte. Cytoplasm abundant, completely surrounds nucleus, pale blue. (A suggestion of fine granules.)

5. Mast cell (*g*): About same size and shape. Nucleus round or oval, very pale blue. Cytoplasm abundant, colorless, mostly to one side of nucleus with purple granules, some scattered over nucleus.

Differential Count, 300 *Cells.*

	Per cent.
Polymorphonuclear with eosinophilic rods	29.6
Polymorphonuclear with eosinophilic granules	4.3
Lymphocyte	42.3
Large mononuclear cell	19.4
Mast cell	2.2
Unclassified cells	2.2
	100.0

AUTOPSY PROTOCOL.

The following findings would correspond to those in a fowl of the average size and weight (1760 gm.) of the animals injected.

Subcutaneous Fat Abundant (Fig. 4). Thick muscle pad covering the skeleton (Fig. 4). Inner surface of skin slightly yellow.

Cervical Lymph-glands * (Figs. 3, a and b). Sometimes difficult to find. Present as two chains, each consisting of six to ten glands, one on each side of neck, lying upon the internal jugular vein, buried in fat, and extending from the middle of neck to base of heart. They are delicate, elliptical, flat, lobulated bodies, averaging 1 x .5 x .2 cm. The parenchymatous lobules are pink and separated from each other by narrow septa of fat. No other lymph-glands were found in the entire body.

Thyroids and Parathyroids.—Two of each gland. The thyroid, a dark red, translucent, spindle-shaped body, 1 x .4 x .4 cm., with just visible colloid-filled acini, separated by delicate gray septa. The parathyroid is attached to its lower pole. This is a small bluish-white sphere, 2 mm. in diameter. Thus, in pairs, they are found, one pair on each side of the body, just above the heart.

Peritoneal Cavity (Fig. 4).—An omentum composed entirely of fat, 1 cm. in thickness, takes its origin from the anterior surface and lower margin of the gizzard, extending over coils of intestine, etc., holding them against the posterior peritoneal wall. It is fastened to the parietal peritoneum, laterally, and at the pubis. The lower margins of the right and left lobes of the liver extend down between the sternum and omentum to within 3 cm. of the tip of the xiphoid.

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* Kon[4] considers these structures the thymus. He[4] and Ellermann[18, 19] state that the fowl has no lymph-glands. Soshestrenski[5] asserts their existence by stating that in his case they were not enlarged.

Liver (Fig. 4).—The first organ which presents itself on removing the sternum. Right lobe measures 7.5 x 4.5 x 2 cm.; left lobe, 6.5 x 5 x 2 cm. Total weight 50 gm. or 2.8 per cent of body weight. Uniformly reddish brown with smooth and glistening surface, soft and friable. Lobule about pin-head in size, center darker than periphery; usually distinct, at times difficult to see. The cut surface shows small blood-vessels on cross and longitudinal section. The lobulation is less readily seen.

Spleen (Fig. 6).—Lies just behind the liver. Measures 2 x 1.5 x 1 cm., weighs 1 gm., or .05 per cent of body weight. It is small, soft, reddish brown. Beneath its smooth and glistening capsule, may be seen bluish white Malpighian bodies, slightly larger than pin-points, at times indistinct. On section, the capsule appears very delicate; trabeculæ are few, but usually definite, containing gaping blood-vessels. Malpighian bodies at times are prominent. Pulp does not rise above edge of capsule.

Heart.—Lies within a delicate, transparent pericardium, containing a small amount of clear serum. Myocardium is uniformly reddish brown.

Lungs.—Bright red and of a characteristic construction, consisting of a mass of entwined air tubules with large lumina and spongy walls, separated from each other by a small amount of vascular connective tissue. On section, this construction becomes more pronounced. The wall of each air tubule projects as a pale ridge, separated from its neighbor by a red linear depression, in which blood-vessels are common.

Gastro-intestinal Tract, Pancreas and Adrenals.—These are of little interest except that beneath the serosa of the lower half of the intestine are frequently seen pearly nodules, less than a pin-head in size.

Mesentery.—A delicate, cobweb-like membrane with some fat, but no demonstrable lymph-glands.

Kidneys.—Measure 6.5 x 1.7 x 1 cm., and weigh together 12 gm., or 7 per cent of body weight. They are uniformly reddish brown with a slightly nodular surface.

Bone-marrow.—Taken from long bones of upper and middle third of leg. It is very soft, semifluid, bright red, mottled with yellow, *i. e.,* rich in red blood cells and fat. Lower part of middle third frequently consists of a solid, yellow column of fat. The marrow cavity may be almost occluded by bony septa.

MICROSCOPICAL EXAMINATION.

Cervical Lymph-gland.—Section shows lobules of parenchyma, separated by fatty tissue. Each lobule is surrounded by a delicate fibrous capsule and contains a very fine reticulum, in which the lymphocyte is diffusely scattered. This is a small, round cell with a round, deeply staining, picnotic nucleus, usually incompletely surrounded by a narrow rim of pink cytoplasm. Sometimes red blood cells are associated with the lymphocyte, but mostly they are confined to and form the sole occupants of the numerous capillaries. They appear as elongated, yellowish-pink cells, with a solid black rod or dot for nucleus, according to whether this is seen in longitudinal or cross section. Scattered through the lobule are small, sharply outlined, hyaline structures, which Kon[4] considered as corresponding to Hassall's corpuscles of the thymus.

Thyroid.—Consists of polyhedral acini, which vary in size, are lined with cubical epithelium and filled with granular colloid. They are separated from each other by a small amount of fibrous tissue, rich in blood capillaries. Sometimes accumulations of lymphocytes may be seen near the larger vessels.

Parathyroid.—Within its capsule is seen a prominent reticulum filled with closely packed cells, whose nucleus is round or oval, semivascular and larger than that of the lymphocyte.

Liver.—The lobule is difficult to limit. Periportal spaces are not easy to find. They consist of one or several arteries, a vein, one or several gall-ducts, and very little or practically no fibrous tissue, usually free from infiltrated cells, although lymphocytes may be present diffusely or in small follicles. The liver cells are arranged in trabeculæ, separated by capillaries. All blood-vessels and capillaries are filled exclusively with red blood cells.

Spleen.—The Malpighian bodies are indistinct, numerous, closely packed, composed of masses of lymphocytes surrounding very small arteries. Red blood cells are limited to the pulp, where they occur more or less in clusters, although one is unable to demonstrate sinuses or inclosures of any kind. The lymphocytes are also diffusely scattered throughout the pulp. Veins tend to be rich in lymphocytes and poor in red blood cells; the artery shows the opposite picture.

Lung.—Presents a characteristic structure, entirely different from that in the human lung. The tubules mentioned in the macroscopical description are seen in cross, oblique, or longitudinal section, forming large polyhedral units with wide walls composed of capillaries. The intercapillary air spaces communicate with each other and with a large central lumen. The latter is lined with a narrow band of smooth muscles surmounted by endothelium, frequently cuboidal. The intertubular fibrous tissue is small in amount, and contains large blood-vessels, whose branches extend into the capillary bed. These structures are closely packed with red blood cells. Only occasionally does one see a lymphocyte. The bronchi resemble those of the human lung. Follicles of lymphoid cells are frequently found in the submucosa or outside of the bronchi near arteries.

Bone-marrow.—A low-power picture is very similar to human resting marrow, *i. e.,* one sees a framework of fatty tissue inclosing nests of marrow cells. Arteries are filled solely with red blood cells. Venous spaces are difficult to determine..

Classification of Marrow Cells.—Very thin paraffin sections were stained with hæmatoxylin and eosin and studied under the oil-immersion lens. The same cells appear slightly different under these conditions than when seen in the Wilson smears of normal and leukæmic blood.

Erythrocytes.

1. Normocyte (*a*) : Elongated, varying in shape, due to pressure. Nucleus a solid, black rod or dot (longitudinal or cross section). Cytoplasm yellowish-pink and glassy.

2. Normoblast (*b*) : Round, diameter about width of normocyte. Nucleus round, uniformly black. Cytoplasm pink or faintly blue, and glassy. Frequently a narrow clear zone is seen about the nucleus.

3. Megaloblast (*b*) : Same, larger, about length of a normocyte. Nucleus slightly picnotic.

Leucocytes.

1. Polymorphonuclear myelocyte with eosinophilic rods * (*c*) : Round, Nucleus, two or more solid black lobes. Cytoplasm colorless with bright red, spindle-shaped rods.

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* These are obviously the polymorphonuclear with eosinophilic rods, the polymorphonuclear with eosinophilic granules and the large mononuclear cell of the normal blood.

2. Polymorphonuclear myelocyte with eosinophilic granules * (*b*): Round, about same size. Nucleus has two or more slightly vesicular lobes. Cytoplasm colorless with bright red granules.

3. Mononuclear myelocyte with eosinophilic granules (*a*): Round, or oval, varying in size, mostly larger than 1 and 2. Nucleus round, oval, or horseshoe-shaped, eccentric, slightly or very vesicular. Cytoplasm colorless with bright red granules.

4. Large mononuclear myelocyte * (*d*): Round, slightly larger. Nucleus round, very vesicular, one or more nucleoli. Cytoplasm basophilic, moderate in amount.

Reticular Cell.—Branched. Nucleus elongated, vesicular, several nucleoli. Cytoplasm pink, giving off delicate fibers to form reticulum.

Lymphocytes, mast cells, platelets, mitoses of red and white cells were not seen. Letters in ( ) = order of predominance.

Heart, Pancreas and Kidney: For all practical purposes similar to the human.

III. A CASE OF SPONTANEOUS LEUKÆMIA.

On October 31, 1912, a typical case of leukæmia of the fowl was brought to the pathological laboratory. The animal, a Plymouth Rock hen, had just been killed, and its body was still warm. Nothing is known of its clinical history. An abstract of the findings is here given.

BLOOD.

The study of the blood was limited to smears taken from the heart just after the animal had been received at the laboratory. They were stained by Wilson's method. A detailed description of the cells of leukæmic blood will be reserved for the experimental leukæmia where far better opportunities for careful study of the same were offered. Suffice it here simply to enumerate and briefly comment upon those cells which were present.

Blood Smears. There was an enormous increase in the white blood cells, the proportion of whites to reds being 1: 1.3. The predominating cells were the large mononuclear and the mononuclear myelocyte with eosinophilic granules. The latter is abnormal to the blood, normal to the bone-marrow, and when extramedullar is typical of leukæmia. Lymphocytes and polymorphs were strikingly decreased. Of the latter those with red granules and the mast cell were rare. Mitoses of the large mononuclear were common. The red blood cells appeared to be poor in hæmoglobin and showed anisocytosis, poikilocytosis and polychromatophilia. These cytoplasmatic changes were usually associated with an increase in the size of the nucleus. Premature red blood cells, normoblasts and megaloblasts were present in large numbers.

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* These are obviously the polymorphonuclear with eosinophilic rods, the polymorphonuclear with eosinophilic granules and the large mononuclear cell of the normal blood.

Differential Count, 300 *Cells.*

	Per cent.
Polymorphonuclear with eosinophilic rods	8
Polymorphonuclear with eosinophilic granules	0
Lymphocyte	2
Large mononuclear cell	30
Mast cell	0
Monuclear myelocyte with eosinophilic granules	52
Unclassified cells	8
	100

AUTOPSY PROTOCOL.

The animal was of medium size; the weight was not taken.

External Appearance.—Comb, featherless area about eyes, and wattles of an ash color. Buccal mucous membrane and conjunctivæ, very pale. Anterior chamber of left eye filled with an old blood-clot. Right eye normal. A moderately firm slightly nodular tumor, 3.7 x 2 x 1.5 cm., occupied the triangular space on the left side of head between the angle of the mouth, ear and angle of the lower jaw, extending below the ramus of the latter. Subcutaneous fat was practically absent. Emaciation was extreme and there was marked muscular atrophy. A second, slightly smaller tumor, 1.7 x 1 x 1 cm., was found just inside the ramus and below the orbit, apparently communicating over the ramus with the first growth and continuous below with a slightly larger, third mass.*

Cervical Lymph-glands.—Somewhat enlarged. Lobulation indistinct.

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* A more detailed description and study of these tumors will be reserved for a future communication.

Peritoneal Cavity.—Omental fat entirely absent. Lower margins of right and left lobes of liver extended almost to the pubes, *i. e.,* far below xiphoid.

Liver.—Enormous. Dimensions and weight not taken. Its surface was extremely mottled. It was reddish brown and specked with innumerable gray or slightly yellow spots from a pin-point to a few millimeters in diameter, frequently closely packed to form irregular areas, the largest 1 cm. in diameter. In addition there were scattered gray or slightly yellow nodules, averaging about 2 mm. in diameter. Sectioned surface similar in appearance. The blood-vessels were surrounded by a gray zone.

Spleen.—Enormous. Dimensions and weight not taken. It was about the size of a small hen's egg. Diffusely gray.

Heart.—At the apex there were several gray spots, pin-point in size.

Kidneys.—Greatly enlarged. Both showed nodules, similar to those in liver.

Bone-marrow.—Abundant, gray, with absence of fat.

Thyroids, Parathyroids, Lungs, Gastro-intestinal Tract, Pancreas and Adrenals.—Apparently uninvolved.

MICROSCOPICAL EXAMINATION.

Cervical Lymph-glands.—The normal structure was somewhat changed. There was complete disappearance of the interlobular fat with approximation of the greatly swollen parenchymatous lobules. Here and there were intra- and inter-lobular foci of myeloid tissue. These frequently enclosed an artery or vein. There was also a more diffuse infiltration of the parenchyma by myeloid cells, filling capillaries, veins, arteries and in places breaking through the lobular capsule into the interlobular tissue. Of the infiltrating cells two predominated: (1) A large mononuclear, usually round, at times slightly polygonal due to pressure, with a single, round, oval, or indented, vesicular, at times multiple, nucleus with one or more nucleoli. Its cytoplasm was non-granular and slightly basophilic. (2) The mononuclear myelocyte with eosinophilic granules, described under normal bone-marrow. Mitoses of these two cells were quite common. Normoblasts and megaloblasts appeared to be present.

Liver.—Here the process was most extreme. Very little liver tissue remained. Everywhere were closely packed masses of myeloid cells from which the liver trabeculæ had completely disappeared. These masses of cells surrounded blood-vessels, both arteries and veins, infiltrating the walls of the latter and filling the lumina of both. Within the vessels the white blood cells were present in about equal proportion with the red blood cells. Between these more focal accumulations the myeloid cells had infiltrated in a more diffuse manner between the liver columns, spreading them apart. It was usually difficult to demonstrate the capillary wall. Hepatic cells in these locations did not suffer so much. Some of the above-mentioned, circumscribed infiltrations showed a coarse sclerosis. The same infiltrating cells were present as in the cervical lymph-glands, with a prevalence of the large mononuclear, which was very rich in mitoses, and the mononuclear myelocyte with eosinophilic granules. The two types of polymorphonuclear cells and the premature red blood cells were present in fewer numbers.

Spleen.—Pulp diffusely infiltrated with closely packed leukæmic cells, which crowded the reticulum, distended the blood-vessels and separated and compressed the Malpighian bodies. The mononuclear myelocyte with eosinophilic granules, although present, was scarce. The large mononuclear, frequently showing mitoses, was the common cell.

Heart.—The intramuscular capillaries, were moderately distended with the large mononuclears and red blood cells, present in about equal proportion. The former had also infiltrated between the muscle fibers. The mononuclear myelocyte with eosinophilic granules was only occasionally seen, both within and without the blood-vessels.

Lungs.—The intertubular blood-vessels, their branches which extend into the capillary bed, and also the capillaries, were distended with leukæmic blood, in which the large mononuclear seemed to exceed the red blood cell. Mitoses were common. Infiltration of the tissue was limited to two foci of myeloid cells. The one was composed principally of the mononuclear myelocyte with eosinophilic granules and the large mononuclear. Mitoses, especially of the first cell, were seen. Both types of polymorphs were also present. The other focus was composed exclusively of premature red blood cells, normoblasts and megaloblasts showing mitoses.

Kidneys.—All the blood-vessels, from the largest to the capillaries of the glomerular tuft, were distended with the characteristic leukæmic blood. Throughout the section there was a diffuse infiltration of myeloid cells, especially between the convoluted tubules. Here and there were foci, in some of which the mononuclear myelocyte with eosinophilic granules predominated, frequently showing mitoses; others seemed to be composed exclusively of the large mononuclear. Here mitoses were also common. In these foci the convoluted tubules had either been pushed aside or had atrophied.

Bone-marrow.—This was greatly changed. It consisted of a closely packed mass of white marrow cells, with complete atrophy of the fat and great rarity of normocytes. One or two small focal areas of sclerosis were present. The arteries were mostly empty. Some showed a little blood containing a few large mononuclears. Those marrow cells, which were present, both red and white, answered to their descriptions given under normal bone-marrow, with the exception of the large mononuclear myelocyte, which showed considerable variation in its nucleus. This was either single or multiple, round, oval, or horseshoe-shaped. The order of predominance had changed greatly. The large mononuclear myelocyte was present in far greater numbers than any other cell, and showed extensive mitoses. The normoblast and megaloblast with mitoses followed next in frequency; then the normocyte. Polymorphonuclear myelocytes, those with eosinophilic rods and those with eosinophilic granules, had disappeared entirely. Curious is the fact that the mononuclear myelocyte with eosinophilic granules could not be demonstrated with certainty. As in the normal marrow lymphocytes, mast cells and platelets were not seen.

Thyroids, Parathyroids, Pancreas and Adrenals.—These were not studied.

SUMMARY.

In summarizing the changes in the blood and organs, there was found:

1. *In the Blood.*—(a) A great increase in the total number of white blood cells. Although a total count was not made, this increase was evident from the appearance of the blood smears, and of the blood-vessels in sections. The actual proportion of white to red cells substantiated this fact. The differential count showed a marked increase of the large mononuclear cell at the expense of the other white blood cells of the normal blood. In addition, a true myelocyte appeared in the circulation. Mitoses of the large mononuclear were common. (b) A corresponding decrease in the total number of red blood cells. These showed a drop in hæmoglobin, variation in size and shape, basophilic staining of the cytoplasm, and swelling of their nuclei. Premature red cells, normoblasts and megaloblasts made their appearance.

2. *In the Organs.*—(a) A diffuse and circumscribed, at times nodular, infiltration of myeloid cells, in which the large mononuclear, and mononuclear myelocyte with eosinophilic granules predominated, although the other cells of the normal bone-marrow were at times present. This myelosis involved especially the liver, spleen, kidneys and bone-marrow, resulting in an extreme enlargement of the first three organs. Almost all of the remaining organs showed infiltrations, but to a less degree. (b) A change in the contents of the blood-vessels. The proportion of white to red cells was greatly increased. The predominating cells were the same as those of the infiltration.

CONCLUSION.

In conclusion, if we consider that the cells, characteristic of both leukæmic infiltrate and blood, were the same, and that under normal conditions the mononuclear myelocyte with eosinophilic granules occurs only in the bone-marrow and the large mononuclear only in the marrow and blood, it is evident from the summarized facts, that the above case must be considered a typical case of *myeloid leukœmia.*

IV. Experimental Leukæmia.

With material from the above case, the disease was successfully transmitted into the fifth generation. A total of 105 animals were used in conducting many different kinds of experiments. Of this number, 22 in all have developed leukæmia. In four additional animals, a definite diagnosis could not be established, although the appearances were highly suggestive. The strain has now been running for more than 13 months.

This paper will be confined to a report of those series which deal with simple transmission of the disease by the injection of an organic emulsion.

Five of these series were conducted, each consisting of 5, 10 or 15 fowls. The percentage of positives per series varied from 20-40 per cent. Of the total number of 40 chickens injected, 13 became leukæmic, *i. e.* 32.5 per cent. In addition, a definite diagnosis could not be made in three, although the findings were very suggestive.

PREPARATION OF MATERIAL, METHODS OF INJECTION, ETC.

The material used for transmission was an emulsion of liver, and sometimes of spleen also. It was prepared by thoroughly macerating pieces of the organ in a mortar, after the addition of .9 per cent normal salt solution. This was filtered through a single layer of fine linen or a small amount of raw cotton, thus removing the fibrous tissue sufficiently for intraperitoneal injection, although, when it was used intravenously, instant death frequently resulted. Hence it was found best to filter also through two layers of filter paper with the aid of a suction pump. This filtrate was found to be absolutely fiber-free, but still contained blood and parenchymatous cells. A 15 per cent emulsion gave the best results. The entire preceding process, as well as the following steps, were carried out aseptically.

The fowls were injected either intravenously or intraperitoneally with 10 cc. Both methods were sometimes combined, when a total of 20 cc. was administered. The vein selected for injection was the large one under the wing.

Animals used for transmission were young, adult hens of the same breed as the spontaneous case, and exemplified by the normal control.

CLINICAL HISTORY.

Incubation Period.—This is usually from five to six weeks. In rare cases, it may reach a maximum of 16 weeks.

Signs and Symptoms.—The onset is usually rather abrupt, preceded by no definite premonitory symptoms. The animal, which has previously appeared entirely normal, begins to show a slight but progressive, at times a sudden and intense, pallor of its comb, the featherless area about the eyes and the wattles. This is almost invariably associated with jaundice, which is likewise progressive and usually reaches an extreme grade. The combination of intense pallor and jaundice results in a characteristic, yellowish-pink color, which gives the fowl a ghastly appearance. The comb may be surprisingly red or extremely pale without jaundice. The animal emaciates rapidly and to an extreme degree. The actual loss in weight during the disease is striking and best illustrated by the following figures. No. 28, on the day of the onset of the disease, weighed 1484.5 gm. The duration of the disease was three weeks, four days. At death the weight was 897 gm. Therefore, there was a loss of 587.5 gm. in 25 days, or at rate of 23.5 gm. per day.

At first the bird acts entirely normally, or it may appear slightly ill. In a few days, however, it acts as if it were very sick, stops eating and drinking, and stands about with head retracted, eyes closed and tail drooping. It prefers to assume a squatting position. If made to move it does so very slowly and carefully. Weakness becomes more and more marked, until on the last day it lies prostrated, with its head on the floor, wings drooping, eyes closed and at times is dyspnœic.

Fever has never been observed.

Duration of the Disease.—This is most frequently from one to two weeks. One case exceptionally acute lasted only 33 hours. Two cases, three days. The longest course was four weeks, four days.

Prognosis.—Having once begun, the disease progresses steadily to a fatal issue. Only in one case out of 23 leukæmic animals did a spontaneous cure result.

BLOOD.

In Gross.—With the onset of anæmia, the vein under the wing collapses and the blood undergoes a change. It soon flows with the greatest ease and rapidity, resembles pale yellow water and shows no tendency to clot. The animal apparently would bleed to death from a pin-point wound, if the hæmorrhage were not artificially arrested.

Blood-count.—In most cases there is a progressive and extreme decrease in the total number of red blood cells. At onset the count may be but slightly below normal, 2,224,000, while just before death it, at times, reaches 630,000. More commonly, the lowest point ranges between 1,112,000 and 1,408,000 per c. mm. In one case, the count remained normal.

The count of white cells is invariably high, between 131,200 and 210,000 per c. mm.

Ratio of $W/R = 1/3 - 1/9$.

Hæmoglobin.—This usually falls steadily and reaches a very low point. From slightly below normal, 40-50 per cent at onset, it frequently drops to 10-15 per cent just before death. In several cases it fell only to 23 per cent. In one case there was no change at all.

Blood Smears.—The morphology of the leukæmic blood is exceptionally interesting. In addition to the enormous increase in the number of white cells, all of the cellular elements show marked changes and many new forms make their appearance. Smears were stained by Wilson's method.

Classification of blood cells (Fig. 2).

Erythrocytes.

1. Normocyte: (a) Normal (*a*), except for variation in the amount of hemoglobin. (b) Showing anisocytosis, poikilocytosis and

polychromatophilia, mostly associated with a swelling of the nucleus and separation of its chromatin (*b*).

2. Normoblast (*c*): Round, diameter less than length of normal normocyte. Nucleus round, of same color or slightly purple, but larger and with more scattered chromatin than nucleus of normal normocyte. Cytoplasm greenish-blue and glassy. Frequently with clear zone about nucleus.

3. Megaloblast (*d*): Same, except diameter equal to or greater than length of normal normocyte.

4. Mitotic Cells (*e*): All stages, from monaster to complete division of nucleus. (a) Round or elliptical, diameter about length of normal normocyte. Dense, deep blue chromosomes, massed in center of cell. Cytoplasm greenish-blue and glassy. (b) Same, with two masses of chromosomes in opposite extremes of cell. (c) Same (at times with a slight constriction in the middle of the cell) with irregular, dense, deep blue or slightly purple chromatin masses in place of individual chromosomes. (d) Same, with two nuclei, similar in appearance to those of normoblast. (e) Same as normal normocyte with two nuclei, similar in appearance to those of normoblast, but only slightly larger than nucleus of normal normocyte. (a), (b), (c) and (d) may show polychromatophilic cytoplasm.

Blood Platelets (*f*).

1. Same as normal, except that cell and nucleus are both larger.
2. Larger than normal with two nuclei.

Leucocytes.

1. Polymorphonuclear leucocyte with eosinophilic rods (*g*): Same as in normal blood, at times possibly a little smaller.

2. Polymorphonuclear leucocyte with eosinophilic granules (*h*): Same as in normal blood, at times possibly a little smaller.

3. Lymphocyte (*i*): Same as in normal blood.

4. Large mononuclear cell: (a) As described in normal blood, with a little less cytoplasm. (b) Same size to one half times larger than (a), with both nucleus and cytoplasm paler (*j*). (a) and (b) cannot be separated absolutely. Every gradation. (c) Mitoses (*k*): All stages, from monaster to complete separation of nucleus. (a′) Elliptical, diameter about one and a half length of normal normocyte. Dense, purple chromosomes centrally massed. Cytoplasm pale bluish-gray,

granular. (b′) Same, with two masses of chromosomes in opposite extremes of the cell. (c′) Same, with two purple nuclei. (d′) Same, with three purple nuclei.

5. Mast Cell (*l*) : As described in normal blood.

6. Mononuclear myelocyte with eosinophilic granules (*m*) : Round or slightly elliptical, diameter about length of normal normocyte or longer. Nucleus, oval, pale blue with dense chromatin, eccentric. Cytoplasm colorless with small and large, bright red granules, some scattered over granules.

Cytoplasmatic Masses without Nuclei (*n*) : Round or slightly oval; diameter varies, usually about width of normal normocyte. No nucleus. Cytoplasm grayish-blue, sometimes with vacuoles.

This, then, is the blood picture common to all the leukæmic cases. The order of predominance of the white cells is typical of leukæmia, differing from the normal, but agreeing with that of the spontaneous case. The large mononuclear is present, by far, in greatest numbers. The other cells of the normal blood are decreased. The polymorphonuclear with eosinophilic granules and the mast cell are very scarce. The mononuclear myelocyte with eosinophilic granules, although not as common as in the spontaneous case, can usually be demonstrated in every leukæmic animal.

The platelets are greatly increased in number.

Differential Count, 300 *Cells.*

	Per cent.
Polymorphonuclear with eosinophilic rods	6
Polymorphonuclear with eosinophilic granules	0
Lymphocyte	4
Large mononuclear cell	86
Mast cell	1
Mononuclear myelocyte with eosinophilic granules	1
Unclassified cells	2
	100

AUTOPSY FINDINGS.

The weight of the animal in every case was far below its weight before injection.* Two lowest weights, at autopsy, were 675 and 897 gm.

External Appearance.—The jaundice was found at times to involve the skin of the entire body.† The conjunctivæ and buccal mucous membranes were always very pale. The eyes, nose and mouth were never involved. There was extreme emaciation, and great scarcity or entire absence of subcutaneous fat. Muscular atrophy was usually marked, at times practically only the skeleton remained (Fig. 5).

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* Animals which remained negative invariably gained in weight.

† Probably this was more frequent but not recognized, except when very grave, because of the normal yellow tint of the skin.

Cervical Lymph-glands.—Macroscopically, these were usually uninvolved. In two cases they were definitely enlarged (Fig. 3, a and b), in the one very much so, measuring 1.5 x 8 x 4 cm. and 2 x 1 x .5 cm., respectively. They appeared uniformly gray. The lobules of the parenchyma were enlarged and the interlobular fat had disappeared. In a third case, they were of normal size and appearance, but showed several gray nodules, 1 mm. in diameter. Microscopically, those glands which appeared normal in gross were usually free from myeloid infiltration, although their blood-vessels contained leukæmic blood. The diffusely enlarged glands showed a marked swelling of their parenchyma, with complete atrophy of the interlobular fat. Myeloid cells, both the large mononuclear and the mononuclear myelocyte with eosinophilic granules, were scattered through the lobules. Foci, some composed entirely of the first, and others exclusively of the second, were localized principally in the interlobular connective tissue. They were rich in mitotic figures. The gray nodules seen in gross proved to be masses of proliferating myeloid cells. All the blood-vessels were filled with the characteristic blood.

Thyroids and Parathyroids.—These were grossly and microscopically uninvolved, with the exception of the blood-vessels, which were filled with leukæmic blood.

Peritoneal Cavity.—In every case the omental fat was greatly decreased. At best, it was present only in moderate amount. As a rule it was replaced by a thin yellow membrane. Ascites occurred in six out of 13 cases, at times in sufficient quantity to distend the abdomen. It was always associated with a sero-fibrinous mass, which covered not only the liver and most of the other abdominal viscera, but also spread over the outer surface of the pericardium.

With enlargement of the liver, the lower margins of its two lobes change their position in relation to the tip of the xiphoid. They descend to this landmark and frequently extend far beyond. With the exception of Nos. 31 and 70, every animal of the 13 had an enlarged liver (Table 1). The margins of the right and left lobes of the smallest of the enlarged livers were, respectively, 1 and 3 cm. above the xiphoid, while the margins of the largest liver extended 3.5 and 3 cm., respectively, below it. In fact, the latter organ *in situ* (Fig. 5) was so enormous that it filled the entire peritoneal cavity and was the only viscus visible on entering the abdomen.

Liver.—As mentioned, the liver was greatly enlarged in 11 cases (Table 1), frequently enormous (Fig. 5). In the smallest of these the right lobe measured 9 x 4.5 x 3.8 cm.; the left lobe, 7 x 5 x 3.8 cm.; in the largest, right lobe 13.5 x 4.5 x 4 cm.; left lobe 12.5 x 4 x 3.5 cm. On comparing them with the normal, these dimensions are not very convincing, with the exception of the length of the lobes. As the organ enlarges, it becomes distorted, because the limited cross-diameter of the peritoneal cavity prevents its expansion in this direction and forces the lobes to follow the costal framework, posteriorly. The long diameters of the lobes are more reliable, because the organ can enlarge freely in this direction.

The weight of the liver is a more accurate indication of its size, especially when expressed in per cent of body weight, *i. e.,* the number of grams of weight of organ per 100 gm. of weight of the animal at death. Thus, the weights were found to range from 80-265 gm, *i. e.,* they were over five times the normal or 6.2-10.3 per cent of body-weight, an increase of 3.6+ times the normal (Table 1).

The external appearance of the liver may not differ much from the normal, but usually it is very characteristic (Fig. 5). It may appear diffusely gray, due to very closely packed subcapsular spots, pin-point to 2 mm. in diameter. These are usually more scattered and translucent, at times slightly yellow and opaque. They may fuse to form larger areas with a diameter of 0.5-1 cm., or they may be arranged in a delicate gray network. In addition, numerous gray or slightly yellow nodules, ranging from 2-0.5 cm. in diameter are often present. The whole gives the surface an extremely mottled appearance. Lobulation at times is visible, usually indistinct. The liver may be slightly firm or friable. The sectioned surface appears very similar to the external surface. Dots and lines often form gray borders along the blood-vessels. The latter also occupy the centers of some of the larger, circumscribed, gray areas. The perivascular connective tissue in rare instances is bile-stained. Microscopically, there is usually a diffuse infiltration of myeloid cells They are closely packed within and without the intralobular capillaries The liver trabeculæ show fatty degeneration and atrophy. The large mononuclear, rich in mitotic figures, is by far the predominating cell.

The mononuclear myelocyte with eosinophilic granules is very scarce. Scattered through the section are also foci of large mononuclears, or of mononuclear myelocytes with eosinophilic granules. Some contain both types of cells. They abound in mitotic figures. The liver cells in these foci have entirely disappeared. The small, gray nodules consist of circumscribed masses of myeloid tissue, usually occupying the periportal spaces and composed of a central portion of large mononuclears surrounded by the mononuclear myelocyte with eosinophilic granules. In the blood-vessels and capillaries, the large mononuclear, at times, seems to greatly exceed the red blood cell in numbers.

Spleen.—Except in Nos. 31 and 70, the spleen in every case was enlarged (Table 1); usually very much (Fig. 6). The dimensions, in contrast to those of the liver, are of definite comparative value. The smallest of the enlarged organs measured 3 x 2 x 1.7 cm., the largest 4 x 3 x 2.3 cm., the latter being just twice the normal in every dimension.

The weights were strikingly increased. The lowest was 6 gm., the highest, 18 gm., *i. e.* 18 times the normal, or .6-1.6 per cent of the body weight, *i. e.*, 32 times the normal.

The surface of the spleen may look normal, be reddish brown and show beneath its capsule pin-point, gray Malpighian bodies. More frequently one sees scattered, gray or slightly yellow spots and nodules (Fig. 6), the first from 1-3 mm., and the largest of the second from 0.5-1 cm. in diameter. Again, the organ appears just diffusely gray. A section (Fig. 6) appears usually the same as the surface. When diffusely gray, the pulp is somewhat granular and bulges. Microscopically, the entire pulp may be diffusely infiltrated with the large mononuclear cell, separating and compressing the Malpighian bodies. In addition, circumscribed, closely packed masses of pure large mononuclears or mononuclear myelocytes with eosinophilic granules are scattered through the section. Again, the myelosis may be present only in foci, with practically no disturbance of the normal splenic structure. Mitoses are abundant wherever the large mononuclear occurs. The contents of the blood-vessels are the same as in the liver.

Heart.—As mentioned above, the external surface of the pericardium is frequently covered with a serofibrinous mass. The heart itself may be somewhat enlarged, otherwise it appears normal (Fig. 5). Microscopically also there is little to be seen besides a great excess of the large mononuclear in the intramuscular capillaries, with an occasional small extravascular focus of infiltration, consisting of the same cell.

Lungs.—These are seldom involved. In two cases they were œdematous. In one, the tubular walls were wide and gray, occluding the lumina. On section, the latter case presented a similar but more marked picture. Microscopically the intertubular blood-vessels, their branches which extend into the capillary bed, and the capillaries themselves, are always filled with leukæmic blood. At times they are greatly distended. The white cells are always increased in number, and sometimes the blood seems to consist solely of closely packed, large mononuclears. Mitoses are everywhere abundant. Very rarely, a few mononuclear myelocytes with eosinophilic granules or large mononuclears are gathered in small masses in the intertubular connective tissue.

Gastro-intestinal Tract, Pancreas and Adrenals.—These in gross showed nothing of interest. No mesenteric lymph-glands were demonstrated. The pancreas, microscopically in no case showed any infiltration of its parenchyma proper, but in several there were numerous nests of myeloid cells in the interlobar fat tissue, usually surrounding one or more capillaries, and composed of the large mononuclear, eosinophilic myelocytes, both mononuclear and polymorphonuclear. Mitoses of both the mononuclears were frequent. The blood-vessels in the parenchyma and fatty tissue contained, as usual, the predominating large mononuclear.

The adrenals also reveal interesting findings histologically. It is quite common for the intertrabecular capillaries to be enormously distended with the characteristic leukæmic blood and for the myeloid cells to have infiltrated between the capillary wall and parenchymatous cells. These nests contain mostly the large mononuclear, but now and again they seem to be very rich in lymphocytes. The parenchyma has suffered greatly; its nuclei stain poorly and frequently its cells show disintegration.

Kidneys.—Of the 13 cases, the kidneys of five were enlarged. The smallest measured 7 x 1.5 x 1.2 cm., the largest 7.2 x 2.2 x 1.4 cm. The weight of both kidneys ranged from 12-26 gm., or 0.8-1.4 per cent of the body-weight. In one case the kidneys were extremely œdematous and weighed 32 gm. or 2 per cent of the body-weight.

The surface and section of the kidney may appear entirely normal, but usually one can see, below its capsule, scattered, gray pin-point dots, delicate lines, or even one or two nodules, the largest 0.5 cm. in diameter. Again, they may appear diffusely gray. In the one case, they were large, succulent and translucent, due to œdema. Microscopically, the kidneys always show more or less distension of their blood-vessels and intertubular capillaries with the characteristic leukæmic blood, in which white blood cells, at times, seem even to exceed the normocytes, and in which the large mononuclear predominates. When capillary distension is moderate, the tubules appear normal; but at times they are so enormously over-filled as to cause extreme atrophy and degeneration of the tubular epithelium, resulting frequently in circumscribed areas devoid of any parenchyma. These areas tend to form a kind of zone about the larger blood-vessels. The glomeruli are surprisingly free. The walls and perivascular tissue of some of the vessels are infiltrated with actively generating myeloid cells, especially the large mononuclear.

Bone-marrow.—This is always involved, usually more or less characteristically, being increased in amount, moderately soft and red, mottled with countless gray dots to slightly larger areas, or it may be diffusely gray. In either case the fat is absent entirely and red blood cells are very scarce. The marrow may be involved as a whole or only in part. Now and again it has been converted into a uniformly gray, dry and slightly firm column, which bulges from the marrow cavity. In such cases it is obviously very rich in white cells, poor in red cells and fat. Microscopically, the normal structure of the marrow is greatly changed. The fatty tissue has completely disappeared and the marrow cells are closely packed in a solid mass, in which the normocyte is rather inconspicuous. The arteries in the center of the marrow are poor in blood. One or two contain a few normocytes and large mononuclears. The description of the red and white cells, which are present agrees with that given under normal marrow. Possibly the large mononuclear is more commonly polygonal, due to pressure. Mitoses of both the large mononuclear and the erythrocytes are common especially the first. The order of predominance has changed from the normal. The large mononuclear myelocyte is present by far in greatest numbers; the normoblast, megaloblast and mononuclear myelocyte with eosinophilic granules follow in about equal numbers; the normocyte comes last. Both types of polymorphonuclear cells, as well as the lymphocyte, mast cells and platelets were not seen at all. Mitoses of the mononuclear myelocyte with eosinophilic granules were not demonstrated.

TABLE 1.—EXPERIMENTAL LEUKÆMIA.

WEIGHTS, IN GRAMS OF BODY, ORGANS AND RELATION OF ORGANS TO BODY AT AUTOPSY.

Animal No.	Body.	Liver.	Liver to body %.	Spleen.	Spleen to body %.	Kidneys.	Kidneys to body %.
Normal	1760	50	2.8	1	0.05	12	0.7
1	1515	117	7.7	11	0.7	20	1.3
6	1200	124	10.3	15	1.2	10	0.8
12	....[1]	95	....	15	....	..	....
14	1573	125	7.9	18	1.1	32[2]	2.0
15	1660	116	6.9	10	0.6	20	1.2
24[3]	....	....	....	..	....	..	....
28	897	85	9.6	6	0.7	..	....
30	1410	107	7.6	17	0.6	..	....
31	675	20	2.9	3	.4	5	0.7
53	....	265	....	12	....	..	....
57	1070	91	8.5	18	1.6	15	1.4
70[4]	....	65	....	4	....	26	....
103	1282	80	6.2	8	0.6	12	0.9

[1] Not weighed.

[2] Very œdematous.

[3] Whole animal kept as a museum specimen. Illustrated, Fig. 5.

[4] Spontaneously cured. Not leukæmic at death.

SUMMARY.

In summarizing the essential points deduced by the simple transmission of leukæmia by the injection of an organic emulsion, we shall consider:

1. *Clinical History.*—After an incubation period, usually from five to six weeks, the fowl suddenly becomes pale, jaundiced, emaciates rapidly, loses weight and shows signs of extreme weakness, followed almost without exception by death in one to two weeks.

2. *Blood.*—(a) The total number of white blood cells is greatly increased, resulting in a proportion of one white to three red blood cells. The differential count shows a marked increase and predominance of the large mononuclear over the other white cells of the normal blood, which have decreased. The mononuclear myelocyte with eosinophilic granules is present in more or less numbers in practically every case. Besides the normal-appearing large mononuclear, one sees many larger, pale forms. In these cells, mitoses, in all stages, typical and atypical, are common. (b) The total number of red blood cells is correspondingly decreased, with a marked fall in the hæmoglobin. They present

variations in size, shape and staining, associated with swelling of the nucleus. Normoblasts, megaloblasts, with mitoses in all stages make their appearance. (c) There is an increase in the number of the blood platelets, associated with an increase both in the size of the cell and the nucleus. The cells frequently contain more than one nucleus. (d) The blood loses its power of clotting.

3. *Organic Findings.*—(a) There is a diffuse, focal, less frequently a nodular infiltration of marrow cells, in which the large mononuclear and mononuclear myelocyte with eosinophilic granules predominate. The foci may be limited to the large mononuclear or granular eosinophilic myelocytes, commonly the mononuclear, or may be composed of both types. Extensive mitoses testify to active proliferation. This myelosis affects most particularly the liver, spleen, kidneys and bone-marrow, causing a great increase in the size of the first three organs. Rarely, the cervical lymph-glands are also very much enlarged. Most of the remaining organs and neighboring tissues may contain infiltrations but not so extensive. (b) The relative proportion of white to red blood cells is greatly increased in the blood-vessels. The same cells predominate as in the infiltrations. (c) There are atrophic and degenerative changes of the parenchyma, general atrophy of the adipose tissue, ascites etc.

CONCLUSION.

The injection of an organic emulsion causes a picture of myeloid leukæmia in every respect similar to that of spontaneous leukæmia as it occurs in the fowl.

The chemical picture and changes produced in the blood and organs are analogous to those which occur in human leukæmia.

V. Conclusion.

1. The spontaneous occurrence of myeloid leukæmia of the fowl is confirmed.

2. Myeloid leukæmia in the fowl is transmissible by the intravenous or intraperitoneal injection of an organic emulsion. The latter is in confirmation of the work by Ellermann and Bang who, as I have stated, were the first to successfully transmit the disease. They were followed by Hirschfeld and Jacoby, whose successful transmissions, however, seem to be limited to a strain, which had its origin in a fowl presented to them by Ellermann and Bang. Burckhardt likewise transmitted the

disease, but here again the stock animal came from Hirschfeld and Jacoby, and therefore indirectly from Ellermann and Bang.

The above reported transmission is of special interest, because it originated from an animal entirely independent and far remote from those of the previous investigators.

LITERATURE OF LEUKÆMIA IN THE FOWL.

1. MOORE, V. A.: Infectious Leukæmia in Fowls—A Bacterial Disease Frequently Mistaken for Fowl Cholera. Twelfth and Thirteenth Annual Reports, Bureau of Animal Industry, U. S., 1895-1896, 185-205.
2. BUTTERFIELD, E. E.: Aleukæmic Lymphadenoid Tumors of the Hen. Folia hæmat., 1905, II, 649-657.
3. WARTHIN, A. S.: Leukæmia of the Common Fowl. Jour. Infect. Dis., 1907, IV, 369-381.
4. KON, J.: Ueber Leukämie beim Huhn. Virchows Arch. f. path. Anat., 1907, CXC, 338-349.
5. SOSHESTRENSKI, N. A.: (Leukæmia of the Chicken.) Uchen. zapiski Kazan. Vet. Inst., 1908, XXV, 215-222.
6. ELLERMANN, V., and BANG, O.: Experimentelle Leukämie bei Hühnern. Vorläufige Mitteilung. Centralbl. f. Bakteriol., 1908, Theil 1, Orig., XLVI, 4-5.
7. ——— Experimentelle Leukämie bei Hühnern. Centralbl. f. Bakteriol., 1908, Theil 1, Orig., XLVI, 595-609.
8. ——— Experimentelle Leukämie bei Hühnern. Verhandl. d. d. path. Gesellsch., 1908, XII, 224-225.
9. ——— (Experimental Leukæmia in Fowls.) Overs. v. d. k. Danske Vidensk. Selsk. Torh., Kbenk., 1908, 65-94; *ibid.*, 1909, p. 261.
10. ——— Experimentelle Leukämie bei Hühnern. Ztschr. f. Hyg. u. Infektionskrankh., 1909, LXIII, 231-272.
11. SCHRIDDE: Gibt es eine infektiose Aetiologie der Leukämie? Deutsche med. Wchnschr., 1909, XXXV, 280.
12. HIRSCHFELD, H., and JACOBY, M.: Zur Kenntnis der übertragbaren Hühnerleukämie. Berl. klin. Wchnschr., 1909, XLVI, 159-160.
13. ——— Uebertragbare Hühnerleukämie. Berl. klin. Wchnschr., 1909, XLVI, 314.

14. Hirschfeld, H., and Jacoby, M.: Uebertragungsversuche mit Hühnerleukämie. Ztschr. f. klin. Med., 1910, LXIX, 107-120.

15. Burckhardt, J. L.: (Bei der 82. Versammlung Deutscher Naturforscher und Aerzte zu Königsberg.) Ztschr. f. Immunitätsforsch. u. exper. Therap., 1910, Theil 2, 810-811.

16. ——— Ueber das Blutbild bei Hühnertuberkulose und dessen Beziehungen zur sogenannten Hühnerleukämie, nebst Bemerkungen über das normale Hühnerblut. Ztschr. f. Immunitätsforsch. u. exper. Therap. 1912, XIV, 544-604.

17. Hirschfeld, H., and Jacoby, M.: Uebertragbare Hühnerleukämie und ihre Unabhängigkeit von der Hühnertuberculose. Ztschr. f. klin. Med., 1912, LXXV, 501-505.

18. Ellermann, V: Undersøgeler over Hønseleukaemiens Virus. Urgesk. f. Laeger, 1913, LXXV, 1685-1691.

19. ——— Untersuchungen über das Virus der Hühnerleukämie. Ztschr. f. klin. Med., 1914, LXXIX, 43-48.

EXPLANATION OF FIGURES.

Fig. 1.—Normal blood of the fowl. Wilson's stain. Zeiss objective 1/12, eye-piece No. 3. Composite picture. (*a*) Normocytes. (*b*) Blood platelets. (*c*) Polymorphonuclear leucocyte with eosinophilic rods. (*d*) Polymorphonuclear leucocyte with eosinophilic granules. (*e*, *e′*) Lymphocytes (small and large). (*f*) Large mononuclear cell. (*g*) Mast cell.

Fig. 2.—Leukæmic blood of the fowl. Wilson's stain. Zeiss objective 1/12, eye-piece No. 3. Composite picture. (*a*) Normal normocytes. (*b*) Normocytes showing anisocytosis, poikilocytosis, polychromatophilia, with swelling of nucleus and separation of its chromatin. (*c*) Normoblast. (*d*) Megaloblast. (*e*) Mitoses of erythrocytes; all stages from monaster to complete division of nucleus. (*f*) Blood platelets; both cell and nucleus increased in size; increase in size with two nuclei. (*g*) Polymorphonuclear leucocyte with eosinophilic rods. (*h*) Polymorphonuclear leucocyte with eosinophilic granules. (*i*) Lymphocyte. (*j*) Large mononuclear cell; same size and larger than normal with both nucleus and cytoplasm paler. (*k*) Mitoses of large mononuclear cell; all stages, from monaster to complete separation of nucleus. (*l*) Mast cell. (*m*) Mononuclear myelocyte with eosinophilic granules. (*n*) Cytoplasmatic masses without nuclei.

Fig. 3.—Cervical lymph-glands of the fowl; normal and leukæmic. Actual size and × 2. Note the great increase in size; replacement of fat by the greatly swollen parenchymatous lobules.

Fig. 4.—Normal fowl with organs *in situ*. Weight, 1750 gm. Note the well-nourished condition of the body; the abundance of fat, subcutaneously,

in the neck, and in the omentum; the large muscles; size of heart and liver.

FIG. 5.—Leukæmic fowl with organs *in situ*. Weight, 1350 gm. Note great emaciation of body; almost entire absence of fat; atrophy of muscles; large heart; enormous liver with the characteristic myeloid infiltrations.

FIG. 6.—Spleen of the fowl; normal and leukæmic, actual size; surface and section. Note the enormous increase in size; in upper half of surface, circumscribed areas of myeloid infiltration; the swollen pulp and infiltrations on section.

DESCRIPTION OF PLATE XX.

Fig. 1.—Normal blood of the fowl. Wilson's stain. Zeiss objective 1/12, eye-piece No. 3. Composite picture. (*a*) Normocytes. (*b*) Blood platelets. (*c*) Polymorphonuclear leucocyte with eosinophilic rods. (*d*) Polymorphonuclear leucocyte with eosinophilic granules. (*e. é*) Lymphocytes (small and large). (*f*) Large mononuclear cell. (*g*) Mast cell.

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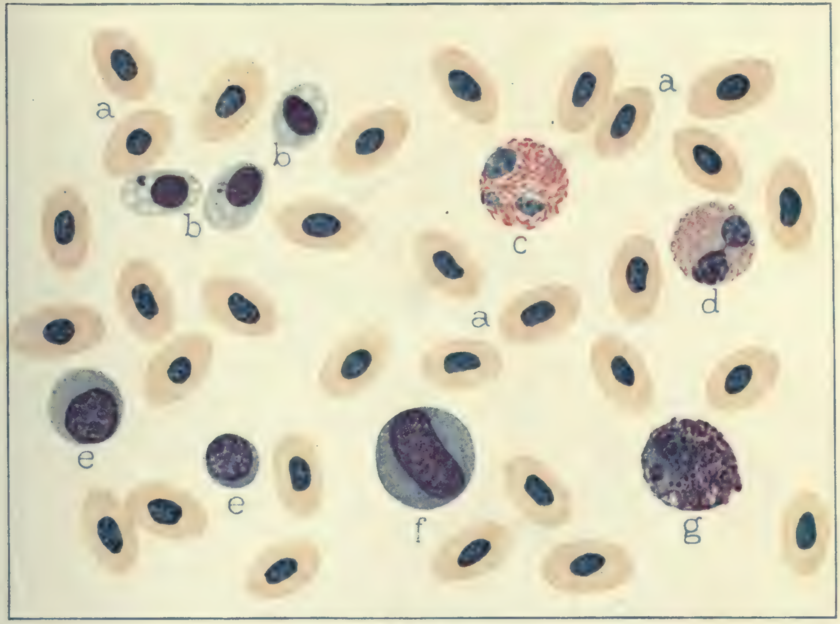

FIG. 1.

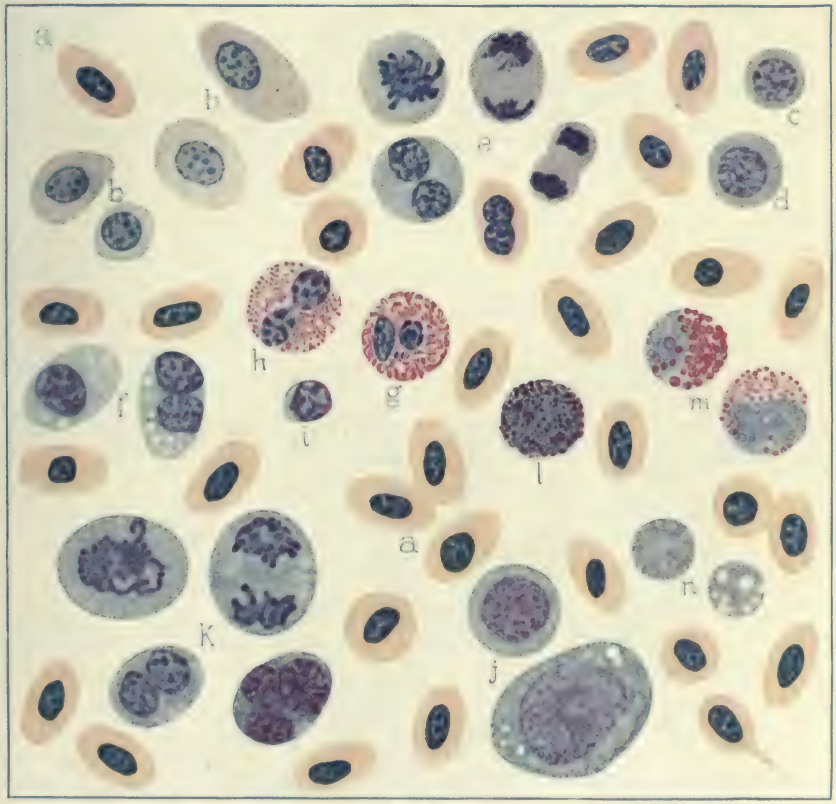

FIG. 2.

Dorothea Pennington *fec.*

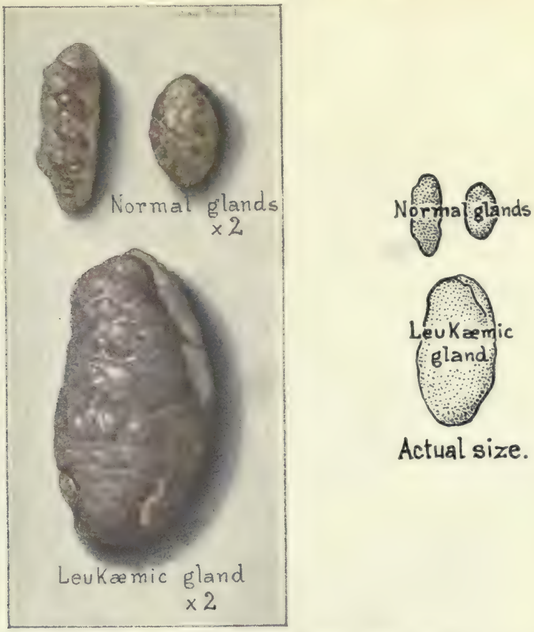

FIG. 3.—Cervical lymphglands of the fowl; normal and leukæmic. Actual size and × 2. Note the great increase in size; replacement of fat by the greatly swollen parenchymatous lobules.

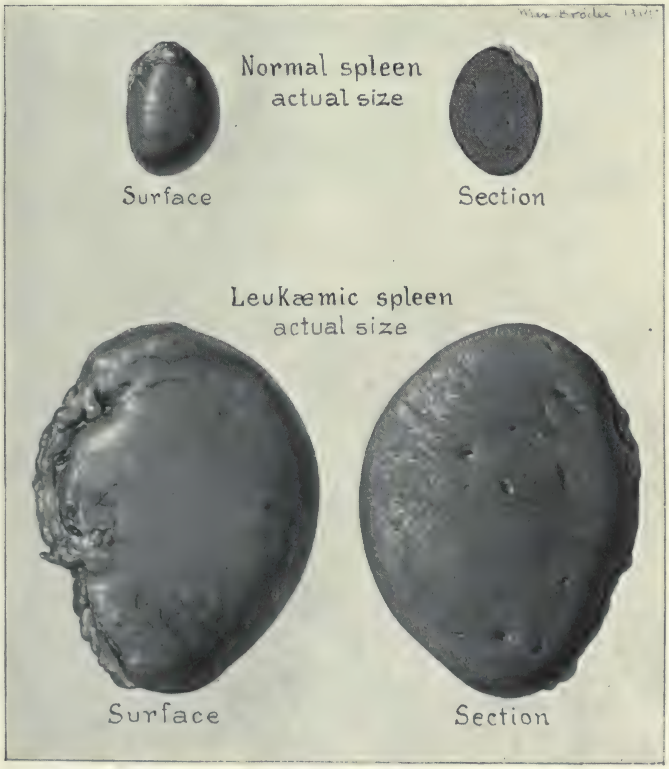

FIG. 6.—Spleen of the fowl; normal and leukæmic, actual size; surface and section. Note the enormous increase in size; in upper half of surface circumscribed areas of myeloid infiltration; the swollen pulp and infiltrations on section.

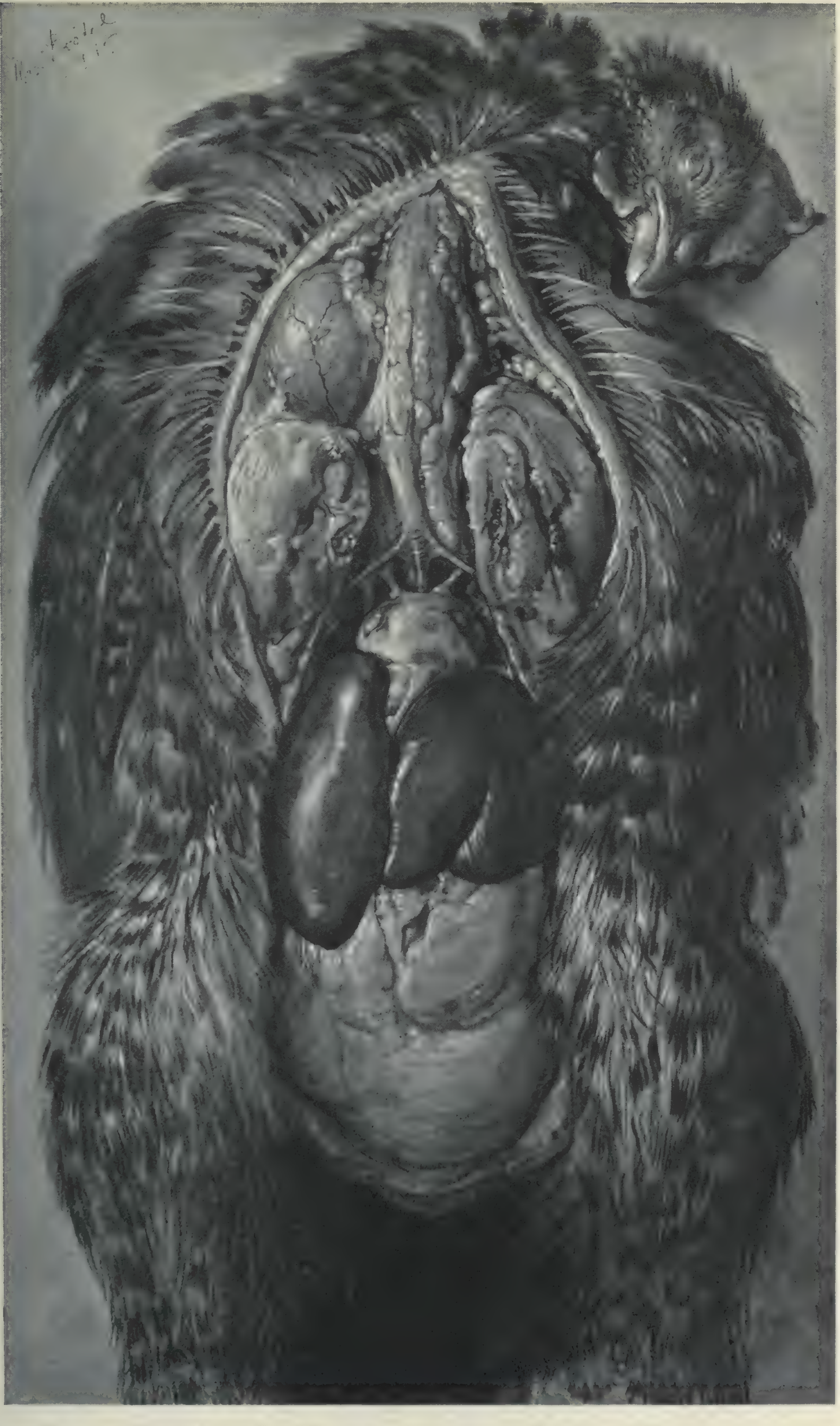

FIG. 4.—Normal fowl with organs *in situ*. Weight, 1750 gm. Note the well-nourished condition of the body; the abundance of fat, subcutaneously, in the neck, and in the omentum; the large muscles; size of heart and liver.

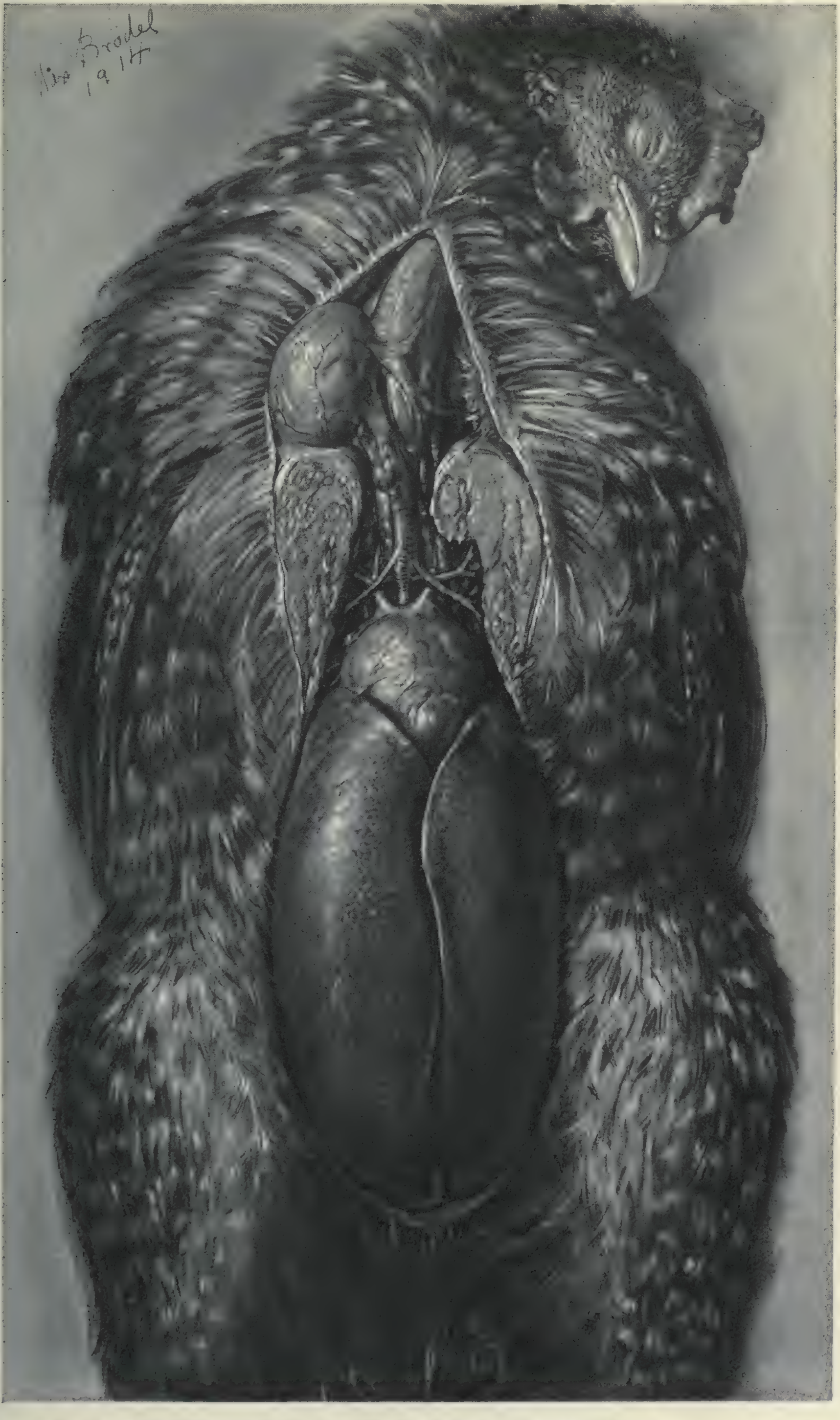

FIG. 5.—Leukæmic fowl with organs *in situ*. Weight, 1350 gm. Note great emaciation of body; almost entire absence of fat; atrophy of muscles; large heart; and enormous liver with the characteristic myeloid infiltrations.

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